Holme Roberts & Owen LLP
Attorneys at Law

COLORADO SPRINGS
BOULDER
DENVER
LONDON
LOS ANGELES
MUNICH
SALT LAKE CITY
SAN FRANCISCO

Via Email

April 16, 2007

Patrice Brunet, Esq.
Brunet Avocats
Place Du Canada
1010, rue de la Gauchetiere Ouest
Suite 2260
Montreal, Quebec H3B 2N2
CANADA

Richard M. McLaren, Esq.
Innovative Dispute Resolution, Ltd.
c/o McKenzie Lake Lawyers, LLP
300 Dundas Street
London, Ontario N6B 1T6
CANADA

Christopher L. Campbell, Esq.
Chapman & Intrieri
2236 Mariner Square Drive
Suite 300
Alameda, CA 94501

Re: *USADA and Floyd Landis*
AAA No. 30 190 00847 06

Dear Panel Members:

Enclosed please find USADA's Pre-Hearing Brief with Exhibits.

Sincerely,

Richard Young

RRY:as

Enclosures

Richard Young richard.young@hro.com
90 South Cascade Avenue, Suite 1300 Colorado Springs, Colorado 80903-1615 *tel* 719.473.3800 *fax* 719.633.1518

BEFORE THE AMERICAN ARBITRATION ASSOCIATION

North American Court of Arbitration for Sport Panel

United States Anti-Doping Agency, Claimant, v. Floyd Landis, Respondent	)	AAA No. 30 190 00847 06

PRE-HEARING BRIEF OF THE UNITED STATES ANTI-DOPING AGENCY

The United States Anti-Doping Agency ("USADA") submits the following Pre-Hearing Brief.

I. INTRODUCTION

Respondent and his legal team may have endeavored to make this the most expensive case in the history of anti-doping, but the scientific issues before the Panel are not unique. Respondent's positive test for testosterone or its precursors[1] was confirmed by Isotope Ratio Mass Spectrometry ("IRMS") – also known as Carbon Isotope Ratio Analysis ("CIR"). IRMS analysis has been used in general science for decades and in anti-doping since the late 1990s. Between 2004 and 2006 the Laboratoire National de Dépistage du Dopage ("LNDD") alone analyzed 362 athlete samples using IRMS, reporting 27 as positive cases. Numerous Court of Arbitration for Sport ("CAS") panels have upheld anti-doping rule violations based on IRMS

[1] For ease of reference throughout the remainder of this brief, USADA will simply refer to doping with testosterone, omitting the phrase "or its precursors."

analysis also going back to the late 1990s. Several of these decision involved IRMS results reported by LNDD.

Moreover, LNDD's decision to declare Respondent's sample positive is also supported by Respondent's testosterone/epitestosterone ("T/E") ratio of 11:1. Respondent's T/E ratio in this sample is more than 600% over his historical T/E ratio established by the mean of 43 other doping control samples provided by Respondent over a four-year period. Longitudinal profiles of an athlete's T/E ratio have been the basis of dozens of scientific publications and many CAS decisions.

As the Panel is aware, Rule 12 of the USADA Protocol for Olympic Movement Testing ("USADA Protocol") prohibits USADA from commenting publicly on the specifics of any pending case. It has been exceedingly frustrating for USADA to endure months of Respondent's misleading press campaign without being able to respond with the truth. For example, two of Respondent's most egregious claims to the press are that Cynthia Mongongu and Esther Cerpolini of LNDD performed analytical procedures on both the A and B sample in violation of the International Standard for Laboratories ("ISL") and that the University of California at Los Angeles ("UCLA") and Sydney laboratories would have declared Respondent's sample negative. As detailed below, both of these claims are simply untrue.

Respondent's initial public response to his positive doping test was to claim that the positive result was caused by thyroid medication, cortisone injections or drinking (Exhibit 39). Respondent's press campaign later evolved into a wholesale attack on the analytical ability of LNDD. LNDD is a World Anti-Doping Agency ("WADA")-accredited laboratory and the inspection of LNDD by the International Organization for Standardization ("ISO") which took

place only five months before Respondent's sample was analyzed expressly certified the same LNDD analytical methods which Respondent is now challenging.

Respondent offers various speculative reasons why LNDD's analytical instruments may not have been operating properly. These theoretical concerns are put to rest by the numerous quality controls run by LNDD. USADA will present detailed evidence during the hearing explaining LNDD's IRMS and T/E ratio methods. Since the Panel is less likely to have substantial experience with IRMS, and to avoid further lengthening of what is already a very long document, USADA will focus this brief primarily on LNDD's IRMS analysis. There is simply no way that LNDD's IRMS instrument could have gotten the correct results on all of the quality control substances run contemporaneously with Respondent's sample but produced erroneous results for Respondent's sample.

IRMS identifies exogenous testosterone use by comparing the $^{13}C/^{12}C$ content of testosterone metabolites to the $^{13}C/^{12}C$ content of an upstream endogenous reference compound that would not be affected by testosterone administration. The ratio of ^{13}C to ^{12}C in each metabolite and endogenous reference compound is described as a delta value. The difference between the delta value of the metabolite and the endogenous reference compound is often referred to as a delta/delta value. The applicable WADA Technical Document provides that doping is proved by "metabolite(s)" with a delta/delta value of -3 or more. The delta/delta values for the testosterone metabolites in Respondent's sample were as follows:

	5 alpha diol – Pdiol	5 beta diol – Pdiol	Andro – 11 ketoetio	Etio – 11 ketoetio
Respondent A sample	-6.14	-2.15	-3.99	-2.58
Respondent B sample	-6.39	-2.65	-3.51	-2.02

Significantly, the delta/delta values of the testosterone metabolites in Respondent's sample are remarkably similar to the delta/delta values of a UCLA research subject who was administered testosterone by injection.

Accordingly, as explained in detail below, the question before this Panel is whether LNDD followed the ISL and relevant WADA Technical Documents in declaring Respondent's sample positive for exogenous steroids. USADA respectfully submits that when the smoke clears from the tireless effort of Respondent's legal and media teams to manufacture distractions and improve Respondent's public image, the Panel will be left with the clear answer that LNDD's analysis followed the ISL and accordingly the presence of exogenous testosterone in Respondent's sample is an anti-doping rules violation.

II. BACKGROUND

A. The UCI Anti-Doping Rules are controlling in this case.

1. The Respondent has acknowledged that the Union Cycliste Internationale ("UCI") Anti-Doping Rules are the controlling rules in this proceeding.[2] USADA agrees and the UCI rules so provide (*See* Exhibit 1, Article 2).

2. The UCI rules recite that UCI has accepted the World Anti-Doping Code ("World Code") and that the World Code is incorporated into UCI's Anti-Doping Rules (Exhibit 1, Introduction, page 1).

3. The UCI Anti-Doping Rules specifically provide that the International Standards adopted by WADA are equally controlling under the UCI rules:

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[2] *See* footnote 1 of Respondent's Rebuttal Brief in Re: Retesting of Urine Specimens that have Previously Tested Negative for Prohibited Substances.

> "Compliance with the *International Standards* (as opposed to other alternative standards, practice or procedure) shall be sufficient to conclude that the procedures addressed by the *International Standards* were performed properly" (Exhibit 1, page 48, Definition of International Standard).

4. The UCI rules in Chapter IX (Exhibit 1, page 31) provide general guidance for the conduct of disciplinary hearings before the license-holder's National Federation (in this case USADA acting on behalf of USA Cycling as required by the Bylaws of the United States Olympic Committee (Exhibit 2, Article 17.2(G))). However, the details of the hearing process are left to the regulations of the license-holder's National Federation (Exhibit 1, Article 230). In this case the regulation which governs the details of the hearing is the USADA Protocol (Exhibit 3). Respondent is also bound to the USADA Protocol by virtue of his UCI license application (Exhibit 28).

B. <u>Burden of Proof</u>

5. It is USADA's burden to convince the Panel to its comfortable satisfaction that Respondent's Sample #995474 was positive for exogenous testosterone (Exhibit 1, UCI Article 16). When an athlete attacks an analytical finding by a WADA-accredited laboratory, the following UCI Rules (incorporated from the World Code) apply:

- **International Standards:**

  Standards adopted by *WADA* in support of the *Code*. Compliance with the *International Standards* (as opposed to other alternative standards, practice or procedure) shall be sufficient to conclude that the procedures addressed by the *International Standards* were performed properly (Exhibit 1, UCI Definitions, page 48).

- **UCI Article 18:**

> *WADA*-accredited laboratories ... are presumed to have conducted *Sample analysis* and custodial procedures in accordance with the *International Standard* for laboratory analysis. The *Rider* may rebut this presumption by establishing that a departure from the *International Standard* occurred.
>
> If the *Rider* rebuts the preceding presumption by showing that a departure from the *International Standard* occurred, then the UCI or the National Federation shall have the burden to establish that such departure did not cause the *Adverse Analytical Finding* (Exhibit 1, UCI Article 18).

6. Accordingly, while the initial burden is USADA's to meet the comfortable satisfaction standard, USADA is aided in meeting that burden by Article 18, which affords a presumption that the analysis conducted on Respondent's samples was done in accordance with the ISL. As a matter of policy, this presumption is supported by the fact that one of WADA's core responsibilities is to monitor the laboratories that it accredits and to ensure that those laboratories are also certified by the ISO. Accordingly, the presumption prevents each arbitration panel from being placed in the position of having to decide accreditation issues related to every procedure performed by the laboratory.

7. Where an athlete can establish that the laboratory performed analysis in violation of the procedures set forth in the ISL, then the athlete has effectively rebutted the presumption under Article 18. Importantly, the definition of "International Standard," as set forth above, conclusively establishes that only deviations from the ISL are relevant to the athlete's attempt to rebut the presumption.

8. Finally, under Article 18, if the athlete is successful in establishing that the laboratory deviated from the ISL, the presumption is rebutted and the burden shifts back to USADA to establish that the departure did not "cause the *Adverse Analytical Finding.*"

C. Chronology

9. **July 20, 2006.** Urine Sample #995474 was collected from Respondent at approximately 5:55 p.m. at the Doping Control Station in Morzine Avoriaz following the 17th stage of the Tour (Exhibit 27). Sample #995474 was transported by courier, helicopter and private plane to Paris and was received by LNDD less than four hours later at 9:35 p.m. (Exhibit 24, USADA 0023-0024).

10. **July 21, 2006.** The A Sample #995474 underwent screening for the prohibited list, including screening for stimulants, diuretics, corticosteroids, EPO, and anabolic steroids. The anabolic steroid screen included an estimate of the T/E ratio at 4.9. Screen data indicated the occurrence of an inhibition of derivatization (the chemical reaction to make steroids more volatile for analysis) (Exhibit 24, USADA 0055).

11. **July 22, 2006**. LNDD began confirmation work from new urine aliquots from the A sample. The confirmation included two parts: T/E and IRMS analysis. In the T/E confirmation, there was a problem with the internal standard (methyltestosterone) being too weak. Therefore, this first T/E confirmation attempt was rejected (Exhibit 24, USADA 0191). LNDD also began the IRMS confirmation on the A sample with the first of three steps in the LNDD IRMS test, namely, sample preparation.

12. **July 23, 2006.** LNDD began a second attempt at T/E confirmation from a new urine aliquot from the A sample. This confirmation was successful. The T/E ratio was 11.4:1 (Exhibit 24, USADA 0101). LNDD also did the second and third of the three steps of the IRMS analysis, the pre-IRMS identification by GC-MS of the six compounds of interest, and the

IRMS analysis. As part of the IRMS analysis, LNDD measured delta values for each of the six compounds of interest, calculated the corrected delta value, and calculated four differences in delta values (delta/delta values) between metabolite and endogenous reference compound (Exhibit 24, USADA 0186):

etio–11ketoetio	-2.58 per mil delta/delta
andro–11ketoetio	-3.99 per mil delta/delta
5 beta diol-pdiol	-2.15 per mil delta/delta
5 alpha diol-pdiol	-6.14 per mil delta/delta

13. **July 25, 2006.** The A sample T/E confirmation vial was reinjected, this time using the screening method. (Remember that there was evidence of incomplete derivatization in the first A screen.) This second A sample T/E screen result was 5.1 (Exhibit 24, USADA 0057). Following the completion of A sample confirmations, LNDD reported an adverse analytical finding on A Sample #995474 to UCI (Exhibit 24, USADA 0188-0189).

14. **July 26, 2006.** UCI notified USA Cycling, with copies to WADA, USADA and Phonak that the sample provided by Respondent on July 20, 2006 had tested positive (Exhibit 41, USADA 0372).

15. **July 27, 2006.** USADA notified Respondent that the sample provided by Respondent on July 20, 2006 had tested positive for an elevated T/E ratio and that the CIR analysis had also been positive, and reported the result positive for exogenous testosterone or its precursors (Exhibit 47, USADA 1138-1142).

16. **July 31, 2006**. Respondent sent a letter to USA Cycling, with copies to UCI, USADA, LNDD and Phonak, requesting the B confirmation (Exhibit 47, USADA 1143-1144). USADA acknowledged the request of Respondent and UCI for the B analysis to be

conducted and sent correspondence to UCI and LNDD confirming that the B analysis would commence on August 3, 2006 (Exhibit 41, USADA 0382).

17. **August 3, 2006.** LNDD began the B sample analysis. It included two parts: T/E and IRMS analysis. The T/E confirmation began on August 3, 2006 with sample preparation and continued with instrumental analysis on August 3 and 4, 2006. The T/E ratio was 11.0:1 (Exhibit 25, USADA 0288). The IRMS B confirmation also began on 3 August 2006. On August 4, 2006, the pre-IRMS identification of the six compounds of interest by GC-MS took place and the IRMS analysis began in order to measure the delta values for each of the six compounds of interest. On August 5, 2006, LNDD calculated the corrected delta values and the four differences in delta values between metabolite and endogenous reference compound (Exhibit 25, USADA 0352):

etio–11ketoetio	-2.02 per mil delta/delta
andro–11ketoetio	-3.51 per mil delta/delta
5 beta diol-pdiol	-2.65 per mil delta/delta
5 alpha diol-pdiol	-6.39 per mil delta/delta

18. **August 5, 2006.** LNDD reported the adverse analytical finding on B Sample #995474 to UCI (Exhibit 25, USADA 0365-0366). UCI then faxed the results of the B sample analysis to USA Cycling, with copies to WADA, USADA, Phonak, and Howard Jacobs (Exhibit 41, USADA 0390-0393).

19. **August 7, 2006.** USADA sent correspondence to UCI requesting the full documentation package for Sample #995474 (Exhibit 41, USADA 0394-0396).

20. **August 23, 2006.** LNDD informed USADA via facsimile that it has sent the full documentation package to USADA via international express mail (Exhibit 41, USADA 0401).

21. **August 30, 2006.** USADA sent correspondence to Respondent, in care of Howard Jacobs, confirming the results of the B Sample analysis, providing Respondent with the relevant rules, the documentation package for the A sample, the documentation package for the B sample, and a copy of the package submitting the case to USADA's independent Anti-Doping Review Board (Exhibit 47, USADA 1145-1148).

22. **September 19, 2006.** USADA sent correspondence to Respondent, in care of Howard Jacobs, informing him that the Anti-Doping Review Board had met and determined there was sufficient evidence of a doping violation and recommended that the adjudication process proceed (Exhibit 47, USADA 1149-1153).

III. SAMPLE COLLECTION AND TRANSPORT

23. Following the completion of the 17th stage of the Tour on July 20th, Respondent appeared at the Doping Control Station in Morzine Avoriaz at 5:50 p.m. (Exhibit 27). The sample collection process at the Morzine Avoriaz Doping Control Station was supervised by a physician, Dr. Bordaberry, and by a delegate of UCI, Mr. Meraviglia. The sample collection process from Respondent was routine and took approximately 10-15 minutes to complete. Before Respondent signed the Doping Control Form, Dr. Bordaberry read each line of it aloud to him, including, for example, the time, date, sample number, density and pH, drugs declared, comments, and the confirmation immediately above Respondent's signature which states: "I declare of honour that the information I have given above is true and I approve the testing procedure." By signing the Doping Control Form without written comment, Respondent, who has been tested many times before, confirmed that:

1. the *Testing* was conducted in accordance with applicable standards and regulations;
2. any subsequent complaint is excluded;
3. he received a copy of the *Testing* form.

(UCI Article 165, Exhibit 1)

24. Dr. Bordaberry put Respondent's A and B specimen bottles in the styrofoam box provided by Berlinger. Dr. Bordaberry then placed the styrofoam box in the refrigerator. After the completion of the testing of the other riders, Dr. Bordaberry, along with Dr. Tonelaere, collected the riders' styrofoam boxes from the refrigerator and put them in a blue cooler with dry ice with the corresponding pink laboratory copies of the Doping Control Forms on top, closed the container, and sealed it with a metal band. (Exhibit 31 is a photograph of a representative sample of the blue cooler sealed with a metal band.)

25. Approximately ten minutes after the completion of Respondent's sample collection, a courier (Mr. David Foulon) employed by the Tour de France (ASO) picked up the cooler containing the samples from Respondent and other riders and drove it directly to an awaiting private helicopter in Morzine. Foulon then entrusted the cooler to Mrs. Esperance Chevalier. Mrs. Chevalier was the hostess employed by ASO during the Tour to accompany VIPs from Paris in the morning to the relevant stages of the Tour and then back to Paris at night by private plane, helicopter or car. Mrs. Chevalier was also responsible for transporting doping control samples from the Tour stages back to the laboratory in Paris. Mrs. Chevalier was responsible for the cooler containing Respondent's sample during the helicopter trip from Morzine to the Annecy Airport and during the airplane flight from Annecy to Paris (Bourget Airport).

26. Mrs. Chevalier was met at the Bourget Airport in Paris by a second courier, Mr. Simonetti (employed by Dynapost, a contracting party from ASO), who was responsible for driving the coolers containing doping control samples from the airport to LNDD

each day. The cooler containing Respondent's sample was handed off by Mr. Simonetti to the laboratory at 9:35 p.m. (Exhibit 24, USADA 0024). The total elapsed time from the moment Respondent arrived at the Doping Control Station in Morzine until his sample was received at LNDD was less than four hours.

IV. IRMS CONFIRMATION OF EXOGENOUS TESTOSTERONE IN SAMPLE #995474

A. LNDD's Adverse Analytical Finding was based on confirmation by IRMS analysis.

27. As reflected on LNDD's Adverse Analytical Finding Reports (Exhibits 24 and 25, pages USADA 0189 and USADA 0366), LNDD based its decision to report Sample #995474 positive based on IRMS confirmation of the presence of exogenous testosterone in Respondent's urine.

B. Applicable rules and legal precedent establishing the IRMS method as independent and definitive proof of the use of exogenous testosterone.

28. Athletes can dope with testosterone or its precursors (e.g., androstenediol, androstenedione, DHEA and testosterone esters) which are metabolized in the body into testosterone. All of these substances are prohibited and are found on the WADA Prohibited List (Exhibit 5) which is incorporated into the UCI Rules (Exhibit 1, Article 21).

29. Until the late 1990s, the method used by WADA-accredited laboratories (previously the IOC-accredited laboratories) to detect testosterone abuse was the T/E ratio. Individuals naturally produce testosterone and epitestosterone in approximately the same quantities. Thus, a normal T/E ratio is approximately 1:1. However, a few individuals have been found to have a naturally elevated T/E ratio. To identify those individuals whose T/E ratio is naturally elevated, Anti-Doping Organizations compare the sample having an elevated T/E ratio against prior or subsequent samples from the same athlete to determine whether the athlete

is consistently elevated (meaning the athlete has an naturally elevated T/E ratio) or whether the subject sample is a spike in T/E ratio (meaning the athlete doped). The T/E ratio considered to be doping or to trigger further investigation has varied. The current ratio triggering the reporting of an adverse analytical finding and required investigation is 4:1.

30. From an anti-doping perspective, there are several limitations to the T/E ratio approach as the exclusive method for detecting doping. First, some athletes' T/E ratio is not very responsive to exogenous testosterone abuse. Thus, they can dope without the ratio ever exceeding 4:1.[3] Second, the T/E ratio approach is not particularly effective in detecting doping with low doses of testosterone. Third, an athlete can mask doping with testosterone by also doping with an appropriate quantity of epitestosterone so that the ratio does not exceed 4:1.

31. Starting in the late 1990s, several of the IOC-accredited laboratories began applying the IRMS method to identify the exogenous use of testosterone.

32. IRMS analysis is now a well established method in anti-doping. The detection of exogenous testosterone using the IRMS method was deemed conclusive proof of doping as early as the 1999 Olympic Movement Anti-Doping Code ("OMADC"). "Evidence obtained from metabolic profiles and/or isotopic ratio measurements may be used to draw definitive conclusions regarding the use of anabolic androgenic steroids" (OMADC, Article 4(2), attached as Exhibit 7). The WADA 2006 Prohibited List (Exhibit 5) which is applicable to this case is equally clear that IRMS findings are definitive proof of doping:

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[3] For example, in USADA v. Hartman, the athlete's sample screened negative using T/E ratio analysis and was reported by the UCLA laboratory as a negative sample. Several weeks later the laboratory went back and conducted IRMS analysis on the sample and detected exogenous testosterone which the athlete subsequently admitted that he had taken (USADA v. Hartman, Exhibit 13, paragraphs 1, 4.1 and 4.2.). See also the UCLA study attached as Exhibit 35 where a number of the research subjects who were administered testosterone did not produce samples with T/E ratios greater than 4:1.

> "In all cases, and at any concentration, the *Athlete's* sample will be deemed to contain a *Prohibited Substance* and the laboratory will report an *Adverse Analytical Finding* if, based on any reliable analytical method (e.g. IRMS), the laboratory can show that the *Prohibited Substance* is of exogenous origin. In such case, no further investigation is necessary."
>
> "If a laboratory reports, using an additional reliable analytical method (e.g. IRMS), that the *Prohibited Substance* is of exogenous origin, no further investigation is necessary and the *Sample* will be deemed to contain such *Prohibited Substance*."

33. Between 2000 and present, at least ten CAS Panels and National Tribunals have found that IRMS analysis is a reliable and definitive method to detect doping with testosterone. For example:

a. In Susin v. FINA the CAS Panel held that even though the T/E ratio in the athlete's B specimen was not reliable because it may have been affected by bacterial degradation, IRMS analysis provided definitive proof of doping:

> "Based upon the above analysis, the Panel has concluded that: (a) the IRMS analysis provides conclusive scientific evidence of an exogenous administration of testosterone and; (b) the Panel is entitled to rely upon the IRMS analysis as an independent and sufficient basis for finding that the Appellant committed a doping offence under FINA Rule DC 2.1(a)" (Susin v. FINA, Exhibit 14, paragraph 220).

b. IAAF v. Dos Santos involved a Brazilian swimmer with an IRMS delta/delta value for a metabolite of approximately -6 (Exhibit 15, paragraphs 11 and 162) which is similar to the Respondent's delta/delta value for the 5 alpha diol metabolite. The CAS Panel concluded:

> "The IRMS analysis provides additional direct and conclusive scientific evidence of an exogenous

administration of the prohibited substance testosterone by the Athlete" (paragraph 88).

In reaching this conclusion the Panel specifically rejected arguments that the IRMS method was not scientifically reliable and that it should be discounted because not all WADA-accredited laboratories were able to perform the method (paragraphs 143-148).

c. In WADA v. Wium the athlete argued that his sample had deteriorated after four days in an unfrozen condition and that the laboratory failed to follow the ISL by not checking for deterioration in the sample. The Panel held that even though it was prepared to assume that there was a departure from the ISL in relation to sample degradation, it made no difference because IRMS analysis is not affected by sample degradation and IRMS independently determines doping (Exhibit 16, paragraphs 6.10-6.14).

d. See also: IAAF v. Czech Athletic Federation and Z (Exhibit 17, paragraphs 27-30); UCI v. S, DCU and DIF (Exhibit 21, paragraph 29); UCI v. Moller (Exhibit 18, paragraphs 11 and 13); UCI v. Bakker and KNWU (Exhibit 19, paragraphs 10.2.6-10.2.14); UCI v. Skelde (Exhibit 20, page 21).

34. There has never been a CAS case where the scientific reliability of the IRMS method to detect exogenous testosterone has not been upheld. Even in UCI v. Landaluce (Exhibit 22), where the doping determination was overturned because the same laboratory personnel had participated in analyzing the A and B samples, the Panel clearly rejected the various challenges raised to LNDD's IRMS method. Respondent is using many of the same arguments that were rejected by the Landaluce Panel. This is not surprising since Mr. Landaluce's expert witness, Dr. de Boer, represented Respondent at his B sample opening (Exhibit 25, USADA 0251 and 0252).

C. **Description of the detection of doping using IRMS.**

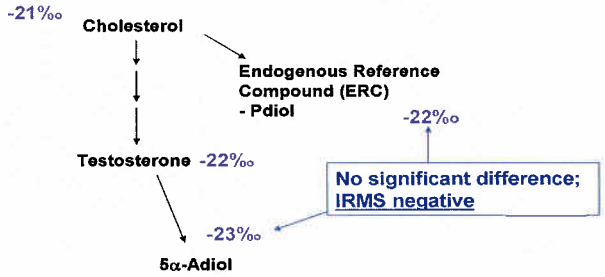
35. Before application to doping control, IRMS had long been used to detect fraudulent substitution of synthetic in place of natural compounds in the food, flavor and fragrance industries. For example, see Exhibit 40 at USADA 1234.

36. In the IRMS method steroids are extracted from urine and separated by a gas chromatograph ("GC"). Each separated steroid enters the combustion furnace where it is completely combusted. Every carbon atom in the molecule is converted to carbon dioxide (CO_2). The CO_2 enters the IRMS instrument. This type of mass spectrometer measures only three masses: 44, 45 and 46. From the three signals, the instrument software calculates the $\delta^{13}C$ (delta) value which reflects the $^{13}C/^{12}C$ (carbon-13 to carbon-12) ratio within the molecule. It is actually the difference between the carbon-13 to carbon-12 ratio of the sample and that of an international standard, a material called PDB. By definition, the delta value of PDB is zero. Natural testosterone contains less carbon-13 than PDB: for example, if it contains 21 parts per thousand less carbon-13 than PDB, then its delta value is -21 per mil (‰). Pharmaceutical testosterone contains even less carbon-13 than natural testosterone: for example, if it contains 29 parts per thousand less carbon-13 than PDB, then its delta value is -29 per mil.

37. The body naturally makes testosterone from cholesterol (which is also a steroid), by converting or "metabolizing" cholesterol to testosterone via many successive steps and intermediate steroids. In addition to this metabolic pathway, there are other pathways branching out from cholesterol to other steroids, some of which are not involved in testosterone metabolism (e.g., 11ketoetio or pdiol). The body also naturally converts testosterone to by-products or "metabolites" with the same carbon framework, but differences in the number of oxygen and hydrogen atoms or their arrangement. In a drug-free person, the natural testosterone might have a delta value of -21, and the delta value of the natural testosterone metabolites won't

be significantly different[4, 5] since the carbon framework remains the same. This is illustrated in Figure 1 below.

Figure 1.
Simplified Illustration of IRMS Test for Testosterone
(No Doping with Exogenous Testosterone)



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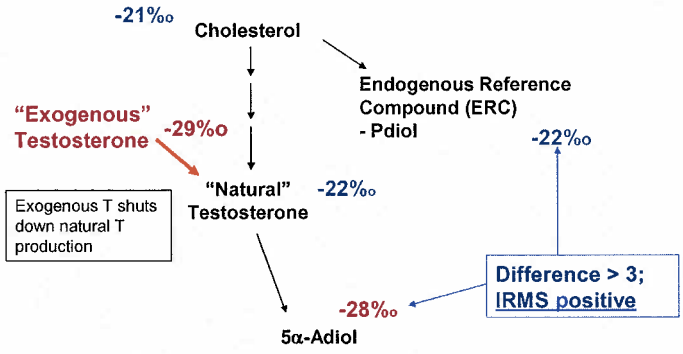
[4] The WADA Technical Document TD2004EAAS defines a significant difference as 3 delta units or more.

[5] Delta values of metabolites are often depleted (more negative, compared to the steroid from which they came) in drug-free persons. When metabolism in the human body converts testosterone to a metabolite, the testosterone molecule and the metabolite molecule that it turns into have literally the very same carbon framework. The difference between the two is in the number of oxygen and hydrogen atoms, or their arrangement. Because the carbon framework remains the same, the carbon-13 to carbon-12 composition remains exactly the same in that one single molecule. Based on this fact alone, one would expect the difference in delta values between testosterone and this metabolite, or between metabolites and endogenous reference compounds, to be zero in drug-free persons. However, the collective research and testing experience of WADA-accredited laboratories shows that differences in delta values in drug-free persons are often different from zero; the results indicate that metabolites contain slightly less carbon-13 than precursors.

The reason for this is a bit complicated; yet it is fully known and understood. It is due to what is called the "isotope effect," which is the simple fact that in nature in general, lighter things are easier to move than heavier things. The human body contains not just one molecule of testosterone, but many millions of them. Although they are all made of 19 carbon atoms in their identical framework, some of them have zero carbon-13 atom and others have one carbon-13 in their framework. The former are lighter. In the biochemical reaction that converts testosterone to its metabolite, the lighter molecules will "move" or react faster, therefore they will be metabolized preferentially, and the metabolite will be depleted in carbon-13. Because this depletion occurs at every step down the biochemical pathway, the further downsteam the metabolite, the more depleted in carbon-13 it tends to be.

In contrast, if a person takes pharmaceutical testosterone, for example, with a delta value of -29, when this pharmaceutical testosterone is metabolized, its carbon framework will remain the same, and the metabolites will have a delta value of -29. In real cases, a given metabolite found in urine might be a mixture of natural and pharmaceutical material; therefore its overall delta value might be somewhere in between, for example, -28. In contrast, the delta values of testosterone precursors, or of endogenous steroids not involved in testosterone metabolism, remain unchanged; therefore they can be used as endogenous reference compounds (ERCs). A significant difference in delta value (>3 units) between a testosterone metabolite and an endogenous reference compound indicates the use of testosterone or of a precursor. This is illustrated in Figure 2 below.

Figure 2.
Simplified Illustration of IRMS Test for Testosterone
(Doping with Exogenous Testosterone)



More sophisticated illustrations of steroid metabolism are found at Exhibit 37.

38. IRMS can establish conclusively that a particular steroid metabolite resulted from the exogenous use of testosterone or one of its precursors.

D. Description of the IRMS method used by LNDD.

39. The LNDD IRMS test consists of three main steps: sample preparation, pre-IRMS compound identification, and IRMS analysis.

40. The first of the three steps in the LNDD IRMS test is sample preparation. It takes all day plus the following night. It includes steps such as extraction, cleavage of sugars attached to the desired compounds by the body's biochemistry, a chemical reaction with a reagent to attach a chemical to the desired compounds to make them easier to vaporize (derivatization as acetates), fractionation into three parts (fractions F1, F2 and F3) for optimal recovery of the six desired compounds: four testosterone metabolites, namely androsterone ("andro"), etiocholanolone ("etio"), 5-beta-androstane-3-alpha,17-beta-diol ("5beta diol"), and 5-alpha-androstane-3-alpha,17-beta-diol ("5alpha diol"); and two endogenous reference compounds, namely 11-ketoetiocholanolone ("11ketoetio," for comparison to metabolites andro and etio) and 5-beta-pregnane-3-alpha,20-alpha-diol ("pdiol," for comparison to metabolites 5beta diol and 5alpha diol). F1 contains 11ketoetio, F2 contains andro and etio, and F3 contains all three diols. Next an internal standard (5-alpha-androstanol acetate) is added for a purpose that will be explained below. Side by side with the sample, a quality control sample undergoes identical steps simultaneously: it is a Blank Urine, previously certified to be negative, and whose measurements are monitored over weeks and months to verify assay performance and results accuracy. In other words, if on any one day the Blank Urine results are as expected, that is one element of proof that the assay is performing correctly on that day.

41. The second of the three steps in the LNDD IRMS test is pre-IRMS compound identification by GC-MS, the gold standard for compound identification in analytical chemistry applications. GC separates the compounds present in a mixture and MS identifies them. The first element of compound identification is the GC "retention time (RT)" and the

second one is the molecular fingerprint recorded by the MS, which fragments the molecule into ions. Compound identification is achieved by matching GC retention times and MS ion patterns (ion ratios) between the compound in the sample and a reference standard.

42. A parameter that is even better than the retention time is the relative retention time (RRT). It relies on the internal standard that was added to each tube during sample preparation. The internal standard has its own characteristic retention time. The relative retention time of any other compound is simply (RT of other compound)/(RT of internal standard). This makes comparisons of retention times easier because it normalizes them.

43. The third of the three steps in the LNDD IRMS test is IRMS analysis. In this step, LNDD measures a delta value for each of six steroids of interest, namely the four metabolites andro, etio, 5beta diol, and 5alpha diol, and the two endogenous reference standards, 11ketoetio, for comparison to metabolites andro and etio, and pdiol, for comparison to metabolites 5beta diol and 5alpha diol. LNDD then calculates four differences in delta values between metabolite and endogenous reference compound: etio–11ketoetio, andro–11ketoetio, 5beta diol-pdiol, and 5alpha diol-pdiol.

E. <u>Sample #995474 A sample IRMS confirmation.</u>

44. The IRMS confirmation on the A sample began on 22 July 2006, and it was done by analyst Cynthia Mongongu (Identification Code 49) under the supervision of Dr. Corinne Buisson (Identification Code 10) as verifying scientist, as seen on pages USADA 0119-0122, 0129, 0130, 0132, 0134, 0136, 0138, 0140, 0142, 0144, 0146, 0155, 0156, 0159, 0162, 0165, 0168, 0171 (Mongongu) and USADA 0151, 0175, 0185-0186 (Mongongu and Buisson).

45. The first of the three steps in the LNDD IRMS test of the A sample, the sample preparation, were performed satisfactorily, as seen on pages USADA 0119-0122.

46. The second of the three steps in the LNDD IRMS test of the A sample, the pre-IRMS compound identification by GC-MS took place on 23 July 2006 (date seen on pages between USADA 0130-0148 and others). Prior to GC-MS analysis of the sample, Ms. Mongongu conducted Verification of GC-MS Instrument Performance. To do this, she followed a procedure that is standard for professionals using GC-MS, and that is used at LNDD before GC-MS steroid screening and before GC-MS T/E confirmation as well. She checked the ion source (the chamber inside the MS where molecules are fragmented into ions for fingerprinting) by tuning the instrument and verifying that the expected ion ratios for the tuning compound were as expected, that a key ion signal was strong enough, and that one particular electrical component didn't need to be cranked way up to get a signal. The failure of any one of these parameters to fall within acceptable range would indicate poor instrument performance and sample analysis would not be attempted; instead the instrument would undergo maintenance or repair. All parameters were good (Exhibit 24, USADA 0146). Next, she did a leak check by verifying that there was no significant air (nitrogen, oxygen, carbon dioxide) and water (ambient moisture in the air) inside the mass spectrometer, as shown by low signal strength within acceptable range. This way, when a compound of interest enters the source, it is essentially the only compound present. This was all satisfactory (Exhibit 24, USADA 0148). Note that this verification was completed on 23 July 2006 around 10:12:58 a.m. (as seen on page USADA 0148, line 3), less than 7 minutes before the first sample in the GC-MS sequence containing Respondent's sample was injected at 10:19 (as seen on page USADA 0130, line 5).

47. The GC-MS sample injection sequence was, as seen on page USADA 0129:

Mix Acetate (reference standards for identification)

Blank Urine fraction F3

Respondent's Sample fraction F3

Blank Urine fraction F1

Respondent's Sample fraction F1

Blank Urine fraction F2

Respondent's Sample fraction F2

48. The Mix Acetate injection has two purposes: to check that the instrument was sensitive enough for the very purpose of the analysis by making sure it could detect reference compounds corresponding to the steroid acetates to be measured; and to record reference standard GC retention times and ion ratios to match with those of the sample. Verification that all the instrument performance parameters fall within the acceptable range individually and all together guarantees that the instrument is functioning properly. Verification of GC-MS Instrument Performance was documented by Ms. Mongongu as seen on page USADA 0146.

49. During the pre-IRMS compound identification, note that for sample Fraction F2, the first injection into the GC-MS was overloaded (in other words, the amount of material exceeded the capacity of the system, which departs from optimal conditions), therefore the sample was diluted and reinjected. The resulting datafile, with a name ending in F2b, gave better data. As proof, see page USADA 0141 (datafile name 17807474F2) where the sailboat shape of the GC peaks indicates overload, and compare to page USADA 0139 (datafile name 17807474F2b) where the GC peaks are substantially more symmetrical.

50. The A sample pre-IRMS compound identification data are shown on pages USADA 0130-0145. For each sample injected, one GC-MS datafile is created, and two pages are included in the documentation package: tables (e.g., page USADA 0130 for the Mix Acetate

reference standards) and chromatograms (e.g., page USADA 0131 for the same reference standards).

51. These are the original data from which compound retention times and ion ratios were recopied onto the summary form on pages USADA 0149-0151.

52. Once the retention times and ion ratios were all entered in the form, the LNDD criteria for compound identification were applied. The LNDD criteria for compound identification are the WADA criteria defined in the WADA Technical Document entitled Identification Criteria For Qualitative Assays Incorporating Chromatography and Mass Spectrometry, TD2003IDCR (Exhibit 12, page 2), as shown on page USADA 0149 (page section immediately below sample number):

Tolérances fixées par l'AMA (document : WADA Technical Document – TD2003IDCR)

Tolérances sur le tr et le trr : +/- 1% ou +/-0.2 min (prendre le plus faible des deux)

Pour les abondances relatives	*>50% il est admis*	*+/-10% (en absolu) de variation*
	25 < ab < 50%	*+/-20% (en relatif)*
	<25%	*+/-5% (en absolu)*

Meaning:

Tolerance defined by WADA (document: WADA Technical Document TD2003IDCR)

Tolerance for the RT and RRT: +/-1% or +/-0.2 min (whichever is smaller)

Relative Abundance	>50% : acceptable	+/-10% variation (absolute)
	25 to 50%	+/-20% (relative)
	<25%	+/-5% (absolute)

Criteria like these have been used in analytical chemistry, either for research or for applications to countless fields for decades. The retention time or relative retention time of the compound in

the sample must fall within the range defined by the retention time or relative retention time (respectively) of the reference compound, plus or minus the required value. The ion ratio for each ion in the compound in the sample must fall within the range defined by the corresponding ion ratio for the reference compound, plus or minus the required value. The evaluation of all data against criteria was all confirmed and documented on USADA 0149-0151 (Exhibit 24). Thus, LNDD identified the six compounds in Respondent's sample according to WADA TD2003IDCR.

53. The third of the three steps in the LNDD IRMS test on the A sample, the IRMS analysis, began on the same day, 23 July 2006, as seen on pages USADA 0122 and 0157 when the fractions were evaporated to dryness, then internal standard and solvent were added. Importantly, there are eight separate quality control measures in place before and during this third step in the IRMS analysis to ensure that the reported results are correct. For the Panel's consideration, each quality control step will be identified with the symbol "✓." On a monthly basis the instrument's linearity is checked. Linearity means that the isotope ratio result is correct whether the signal is small, medium or large. Linearity was checked on June 26, 2006 before the analysis of Respondent's A sample (Exhibit 26, LNDD 0313-0319)✓[1]. Prior to IRMS analysis of the sample, Ms. Mongongu began conducting Verification of the IRMS Instrument Performance. She checked that the instrument pressure was within the acceptable range✓[2]. She tuned the instrument to make sure it was focused on the target masses✓[3].

54. She then began the sequence of injections, seen on page USADA 0155:

Stabilite 1

Stabilite 2

Stabilite 3

Mix cal IRMS 003-1

Mix cal IRMS 003-2

Mix cal IRMS 003-3

Mix Cal Acetate (reference standards)

Blank Urine fraction F3

Respondent's Sample fraction F3

Blank Urine fraction F1

Respondent's Sample fraction F1

Blank Urine fraction F2

Respondent's Sample fraction F2

Mix Cal Acetate (reference standards)

55. She checked stability *(stabilite)*, by injecting carbon dioxide several times in a row to make sure that repeated measurements were reproducible within the specified tolerance. They were (USADA 0174)✓[4]. She checked precision, by injecting one vial of Mix Cal IRMS (reference standard alkanes) three times in a row, again to make sure that the triplicate results were consistent. They were (USADA 0174)✓[5]. She checked calibration and accuracy, by injecting Mix Cal Acetate (reference standard steroid acetates), to make sure that LNDD measurements on this day agreed with reference laboratory (Eurofins) measurements of the exact same reference standards against international standard PDB. They did (pages LNDD 0298, 0301, 0304, 0307)✓[6]. All these checks individually and together ensured that the subsequent sample measurements were accurate. Respondent's sample and Blank Urine Fractions F3, 1, and 2 were then injected. The four delta/delta values for the Blank Urine were compared to the expected value for that Blank Urine pool✓[7]. The final injection in the sequence is also the second injection of Mix Cal Acetate. This step provides data that establish that the instrument has remained stable from the first Mix Cal Acetate injection to the second Mix Cal Acetate

injection, in other words, throughout all the Blank Urine and Respondent's sample injections. Indeed, the second set of Mix Cal Acetate (reference standard steroid acetates) measurements on this day also agreed with reference laboratory (Eurofins) measurements of the exact same reference standards (USADA 0175)✓[8].

56. Ms. Mongongu's instrument performance verification was approved by her verifying scientist, Dr. Buisson, as seen at the bottom of page USADA 0175. Only after verifying that instrument performance verification is complete and satisfactory are the quality control and sample data accepted and read.

57. The quality control and sample IRMS data are shown between pages USADA 0157 and 0184. For each sample injected, one IRMS datafile is created, and two pages are included in the documentation package: the chromatogram (e.g., page USADA 0158 for the Blank Urine, Fraction F1) and the corresponding tables (e.g., page USADA 0157).

58. The tables show the raw data, including the delta values, that were entered in the summary form on pages USADA 0185-0186. Once the delta values were all entered in the summary form, they were "corrected." Recall that during sample preparation, the compounds of interest were subjected to a chemical reaction to attach a chemical to make them easier to vaporize for analysis. The chemical that was attached (acetate) contains two carbon atoms, with a certain proportion of ^{12}C and ^{13}C, which is known to LNDD because LNDD determined it during validation (Exhibit 26, pages LNDD 0502-0505 and the article found at Exhibit 26, LNDD 0478, page 645). To determine the delta value in the absence of the added acetate, LNDD calculates the corrected delta value. The corrected delta values appear immediately below the measured delta values in the tables on pages USADA 0185. Next LNDD calculated

the final results, namely the four differences in delta values between metabolite and endogenous reference compound, and recorded them as seen on page USADA 0186:

etio–11ketoetio	-2.58 per mil
andro–11ketoetio	-3.99 per mil
5betadiol-pdiol	-2.15 per mil
5alphadiol-pdiol	-6.14 per mil

59. LNDD criteria for positivity were then applied. The LNDD positivity criteria are the WADA criteria defined in the WADA Technical Document TD2003IDCR, as shown on page USADA 0186 (above "**Conclusion**"):

Seuil de positivité de l'AMA: $\delta^{13}C‰$*(métabolite)* - $\delta^{13}C‰$*(composé endogène de référence) > 3‰*

$\delta^{13}C$ *du composé <-28‰*

WADA positivity cutoff: $\delta^{13}C‰$(metabolite) - $\delta^{13}C‰$(endogenous reference compound) > 3‰

compound $\delta^{13}C$<-28‰

60. LNDD concluded that an adverse analytical finding should be reported for the A sample according to WADA TD2004EAAS.

F. Sample #995474 B IRMS confirmation.

61. The IRMS confirmation on the B sample began on 3 August 2006, and it was done by analyst Claire Frelat (Identification Code 26) under the supervision of Cynthia Mongongu (Identification Code 49) as verifying scientist, as seen on pages USADA 0299-0302, 0308, 0309, 0311, 0313, 0315, 0317, 0319, 0321, 0326, 0332, 0336, 0339, 0342, 0345, 0348 (Frelat) and USADA 0294, 0325, 0351+0352, 0354 (Frelat and Mongongu).

62. The first of the three steps in the LNDD IRMS test of the B sample, the sample preparation, was performed satisfactorily, as seen on pages USADA 0299-0301.

63. The second of the three steps in the LNDD IRMS test of the B sample, the pre-IRMS compound identification by GC-MS took place on 4 August 2006 (date seen on pages between USADA 0309-0321 and others). Prior to GC-MS analysis of the sample, Ms. Frelat conducted Verification of GC-MS Instrument Performance, in the same way as Ms. Mongongu for the A confirmation. Ms. Frelat checked the ion source by tuning the instrument and verifying that the key ion ratios, signal strength, and voltage fell in the acceptable range. Next, she did a leak check by verifying that there was no significant air (nitrogen, oxygen, carbon dioxide) and water (ambient moisture in the air) inside the mass spectrometer, as shown by low signal strength within acceptable range. This was satisfactory. Note that this verification was completed on 4 August 2006 around 08:27:34 a.m. (as seen on page USADA 0328, line 3), less than one hour and 16 minutes before the first sample in the sequence containing Respondent's sample was injected at 09:43 (as seen on page USADA 0130, line 5).

64. The GC-MS sequence of sample injections was, as seen on page USADA 0308:

Mix Acetate (reference standards for identification)

Blank Urine fraction F3

Respondent's Sample fraction F3

Blank Urine fraction F1

Respondent's Sample fraction F1

Blank Urine fraction F2

Respondent's Sample fraction F2

65. The Mix Acetate injection has two purposes: to check instrument sensitivity and to record reference standard GC retention times and ion ratios. Verification that all the instrument performance parameters fall within the acceptable range individually and all

together guarantees that the instrument is functioning properly. Verification of GC-MS Instrument Performance was documented by Ms. Frelat as seen on page USADA 0326.

66. For each sample injected, one GC-MS datafile is created, and two pages are included in the documentation package: tables (e.g., page USADA 0309 for the Mix Acetate reference standards) and chromatograms (e.g., page USADA 0310 for the same reference standards).

67. These are the raw data from which compound retention times and ion ratios were recopied onto the summary form on pages USADA 0323-0325.

68. Once the retention times and ion ratios were all entered in the form, the LNDD criteria for compound identification which are the WADA criteria defined in the WADA Technical Document were applied as set forth in paragraph 52 above. The matches were all observed and documented on USADA 0323-0325 (Exhibit 25). Thus, LNDD identified the six compounds in Respondent's sample according to WADA TD2003IDCR.

69. The third of the three steps in the LNDD IRMS test of the B sample, the IRMS analysis, began on the same day, 4 August 2006, as seen on pages USADA 0302 and 0333, when the fractions were evaporated to dryness, then internal standard and solvent were added. After the B confirmation of Respondent's A sample and before the confirmation of Respondent's B sample, the linearity of the instrument was checked again on July 31, 2006. Linearity was checked again after Respondent's B sample analysis on September 25, 2006 (Exhibit 26, LNDD 0320-0332)✓[1]. Prior to IRMS analysis of the sample, Ms. Frelat began conducting Verification of the IRMS Instrument Performance. She checked that the instrument pressure was within the acceptable range. It was (USADA 0355)✓[2]. She tuned the instrument to make sure it was focused on the target masses. It was (USADA 0353)✓[3].

70. She then began the sequence of injections, seen on page USADA 0331:

Stabilite 1

Stabilite 2

Stabilite 3

Stabilite 4

Stabilite 5

Mix cal IRMS 003-1

Mix cal IRMS 003-2

Mix cal IRMS 003-3

Mix Cal Acetate (reference standards)

Blank Urine fraction F3

Respondent's Sample fraction F3

Blank Urine fraction F1

Respondent's Sample fraction F1

Blank Urine fraction F2

Respondent's Sample fraction F2

Mix Cal Acetate (reference standards)

71. She checked stability, by injecting carbon dioxide several times in a row to make sure that repeated measurements were reproducible within the specified tolerance. They were (USADA 0353)✓[4]. She checked precision, by injecting one vial of Mix Cal IRMS (reference standard alkanes) three times in a row, again to make sure that the triplicate results were consistent. They were (USADA 0353)✓[5]. She checked calibration and accuracy, by injecting Mix Cal Acetate (reference standard steroid acetates), to make sure that LNDD measurements on this day agreed with reference laboratory (Eurofins) measurements of the exact same reference standards. It did (Exhibit 26, pages LNDD 0298, 0301, 0304, 0307 and

Exhibit 25, USADA 0354)✓[6]. All these checks individually and together ensured that the subsequent sample measurements were accurate. Blank Urine Fractions F3, 1, and 2 were injected before each injection of Respondent's sample. The four delta/delta values from the Blank Urine matched the expected values✓[7]. The final injection in the sequence is also the second injection of Mix Cal Acetate. It gives data that prove that the instrument has remained stable from the first Mix injection to the second Mix injection, in other words, throughout all the Blank Urine and Respondent's sample injections (USADA 0354)✓[8]. Indeed, the second set of Mix Cal Acetate (reference standard steroid acetates) measurements on this day must also agree with reference laboratory (Eurofins) measurements of the exact same reference standards against international standard PDB.

72. Ms. Frelat's instrument performance verification was approved by her verifying scientist, Ms. Mongongu, as seen at the bottom of page USADA 0354. Only after verifying that instrument performance verification is complete and satisfactory are the quality control and sample data accepted and read.

73. The quality control and sample data are shown between pages USADA 0333 and 0350. For each sample injected, one IRMS datafile is created, and two pages are included in the documentation package: the chromatogram (e.g., page USADA 0333 for the Blank Urine, Fraction F1) and the corresponding tables (e.g., page USADA 0335).

74. The tables show the raw data, including the delta values, that were entered in the summary form on pages USADA 0351-0352. Once the delta values were all entered in the summary form, they were "corrected" as previously explained at paragraph 58. The corrected delta values appear immediately below the measured delta values in the tables on pages USADA 0351. Next LNDD calculated the final results, namely the four differences in delta

values between metabolite and endogenous reference compound, and recorded them as seen on page USADA 0352:

etio–11ketoetio	-2.02 per mil
andro–11ketoetio	-3.51 per mil
5betadiol-pdiol	-2.65 per mil
5alphadiol-pdiol	-6.39 per mil

75. LNDD criteria for positivity were then applied. The LNDD positivity criteria are the WADA criteria defined in the WADA Technical Document TD2004IDCR, as shown on page USADA 0186 (above "**Conclusion**"):

Seuil de positivité de l'AMA: $\delta^{13}C‰$*(métabolite) -* $\delta^{13}C‰$*(composé endogène de référence) > 3‰*

$\delta^{13}C$ *du composé <-28‰*

WADA positivity cutoff: $\delta^{13}C‰$(metabolite) - $\delta^{13}C‰$(endogenous reference compound) > 3‰

compound $\delta^{13}C$<-28‰

76. LNDD concluded that an adverse analytical finding should be reported for the B sample according to WADA TD2004EAAS.

G. The standards and controls which LNDD ran contemporaneous with the analysis of the Landis A and B samples and other instrument checks performed by LNDD establish that the results reported by LNDD are reliable.

77. Respondent's speculation that the IRMS instrument may not have been operating properly during the analysis of Respondent's A or B sample is entirely put to rest by the instrument checks performed before the analysis of this sample and the precision and accuracy of the result of controls run contemporaneously with the samples. The Verification of IRMS Instrument Performance which occurred prior to and during Respondent's sample analysis was not only excellent on the day of the A confirmation and on the day of the B confirmation,

but it was also reproducible between those two days and was exceptionally consistent with prior measurements using the same standards and controls. This is demonstrated by the results obtained for the Mix Cal standard, the Mix Cal Acetate standard, and the standard Blank Urine during the analysis of Respondent's A and B samples. The results for each of these controls will be discussed separately below.

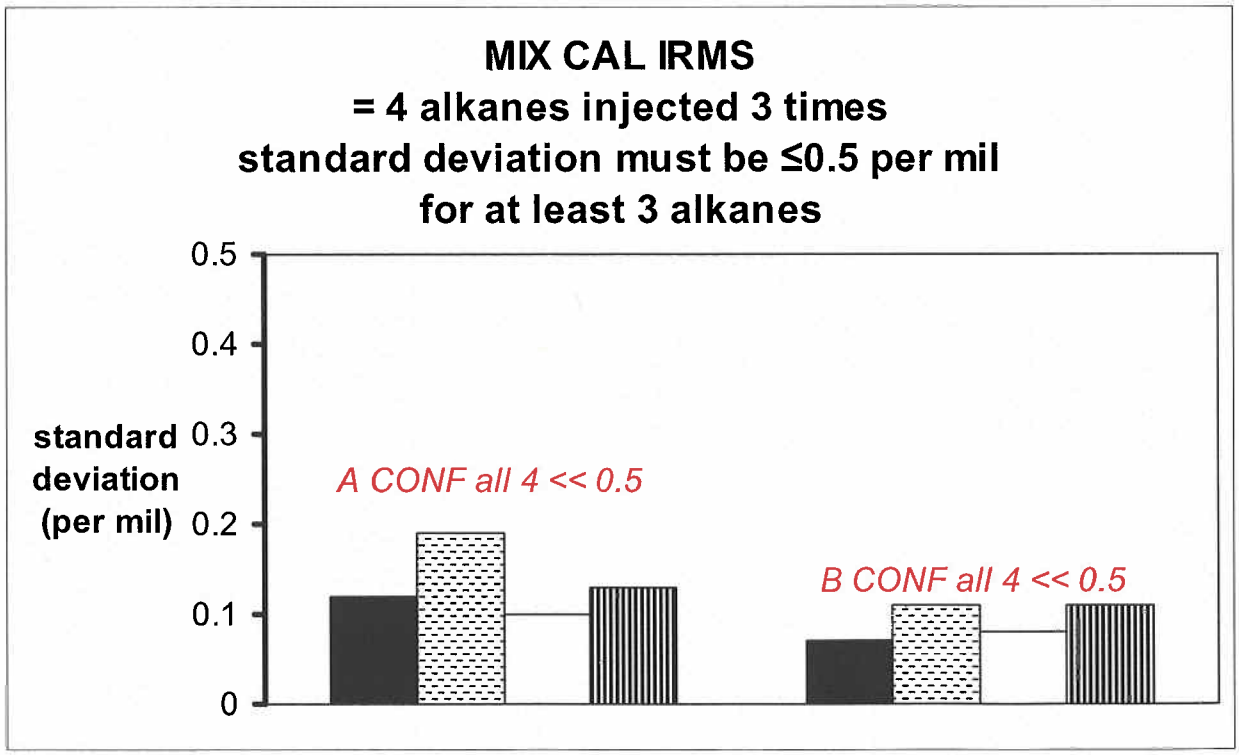
78. The Mix Cal IRMS control contains four different alkane standards (compounds made of only carbon and hydrogen atoms, commonly used to verify analytical instrument performance). LNDD checks precision by injecting one vial of Mix Cal IRMS three times in a row, to make sure that the triplicate results (delta values) are tight. For each of the four alkanes (decane, undecane, dodecane, methyldecanoate), LNDD calculates the mean delta value and standard deviation. The criterion for acceptability is that the standard deviation must be less than or equal to 0.5 per mil for at least three of the four alkanes in the mix. This criterion was met on the day of the A confirmation and on the day of the B confirmation. There is also good consistency between the A confirmation and the B confirmation data.

Figure 1

MIX CAL IRMS Delta values (per mil)					
A sample IRMS confirmation					
Data filename	decane	undecane	dodecane	methyldecanoate	Delta values: USADA page
DATA_004	-32.52	-28.45	-31.96	-31.51	0178
DATA_005	-32.74	-28.28	-32.13	-31.76	0179
DATA_006	-32.56	-28.65	-31.95	-31.59	0180
B sample IRMS confirmation					
Data filename	decane	undecane	dodecane	methyldecanoate	Delta values: USADA page
DATA_006	-32.30	-27.78	-31.79	-31.30	0357
DATA_007	-32.44	-27.99	-31.93	-31.44	0358
DATA_008	-32.33	-27.81	-31.80	-31.22	0359

The precision established by the Mix Cal control is illustrated in Figure 2.

Figure 2



79. LNDD's Mix Cal Acetate control is a mixture of four steroids: 5α-Androstanol, Etiocholanolone, 5β-Androstanediol and 11-Ketoetiocholanolone. The delta value of each of the four steroids in LNDD's Mix Cal Acetate control mix was previously verified by an external reference laboratory, Eurofins. The exact values established by Eurofins are found at Exhibit 26, pages LNDD 0298, 0301, 0304, 0307. LNDD uses the Mix Cal Acetate control to check instrument accuracy. LNDD's criteria for acceptability is that at least three of the four measurements from the control must agree with the Eurofins measurement ±0.5 per mil. This criteria was met on the day of Respondent's A sample analysis and on the day of Respondent's B sample analysis. In addition, the A sample results and B sample results were consistent with each other as shown on Figure 3 below.

Figure 3. Accuracy of Mixed Cal Acetate δ Values

	5α-Androstanol	Etiocholanolone	5β-Androstanediol	11-Ketoetiocholanolone
"True" Value from Eurofins	-30.46 ‰	-19.91 ‰	-33.81 ‰	-16.30 ‰
7/24 immediately before Respondent's sample	-30.29 ‰	-20.01 ‰	-33.70 ‰	-16.69 %
7/24 immediately after Respondent's sample	-30.56 ‰	-20.22 ‰	-33.90 ‰	-16.76 ‰
8/4 immediately before Respondent's sample	-30.40 ‰	-19.98 ‰	-33.71 ‰	-16.74 ‰
8/4 immediately after Respondent's sample	-30.25 ‰	-19.95 ‰	-33.63 ‰	-16.68 ‰

As illustrated in Figures 4 and 5 below, the four steroids in the Mix Cal Acetate standard have delta values spread over a large range from approximately -16 delta units to -33 delta units. This large spread proves that LNDD's measurements are accurate not only around -16 delta units but also around -33 delta units and for every value in between. All six delta values for the testosterone metabolites and endogenous reference compounds measured in Respondent's sample fall within that range (six red triangles). Since the LNDD delta values were correct for the known Mix Cal Acetate compounds, then the LNDD delta values are also correct for the six compounds in Respondent's sample.

Figure 4

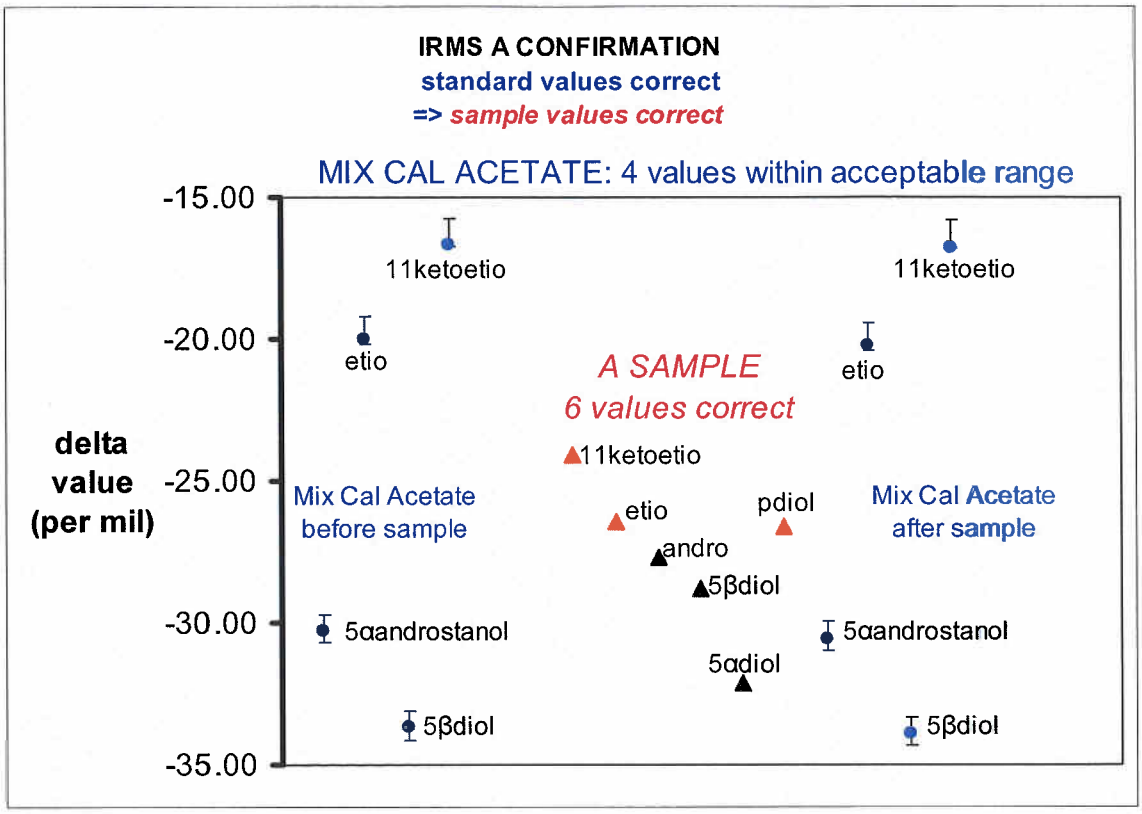
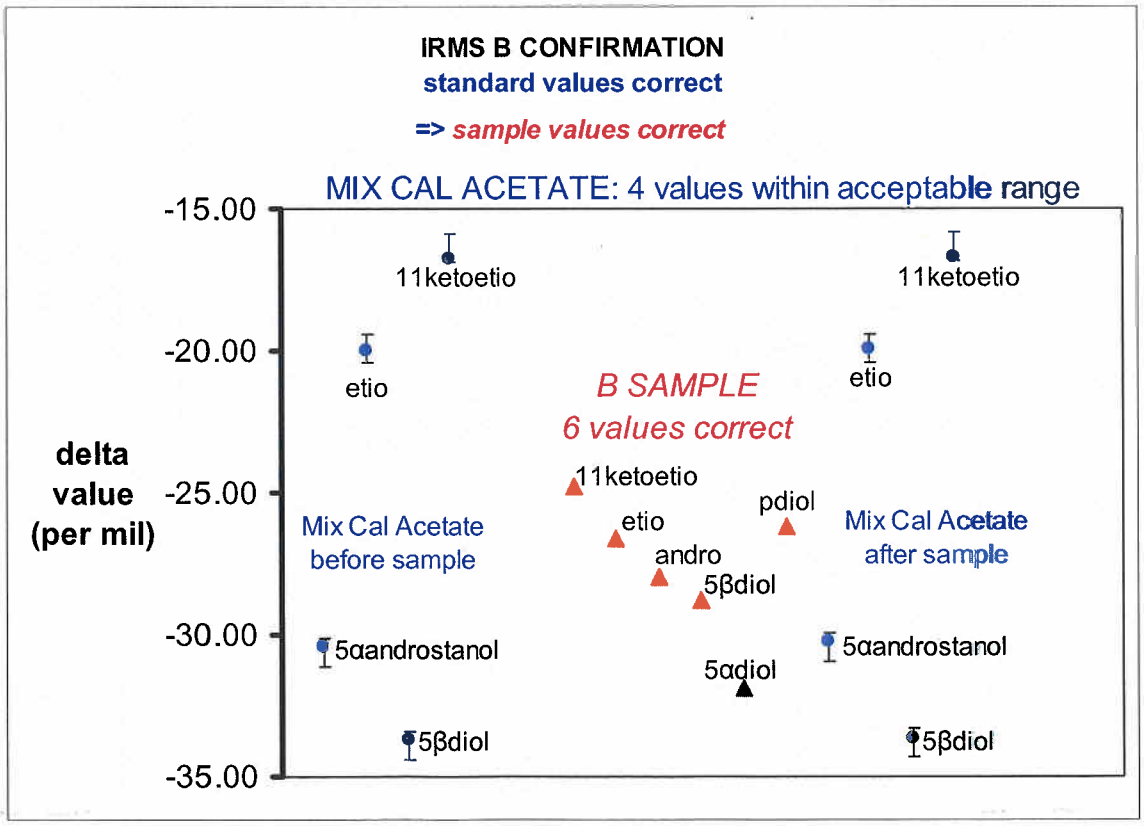
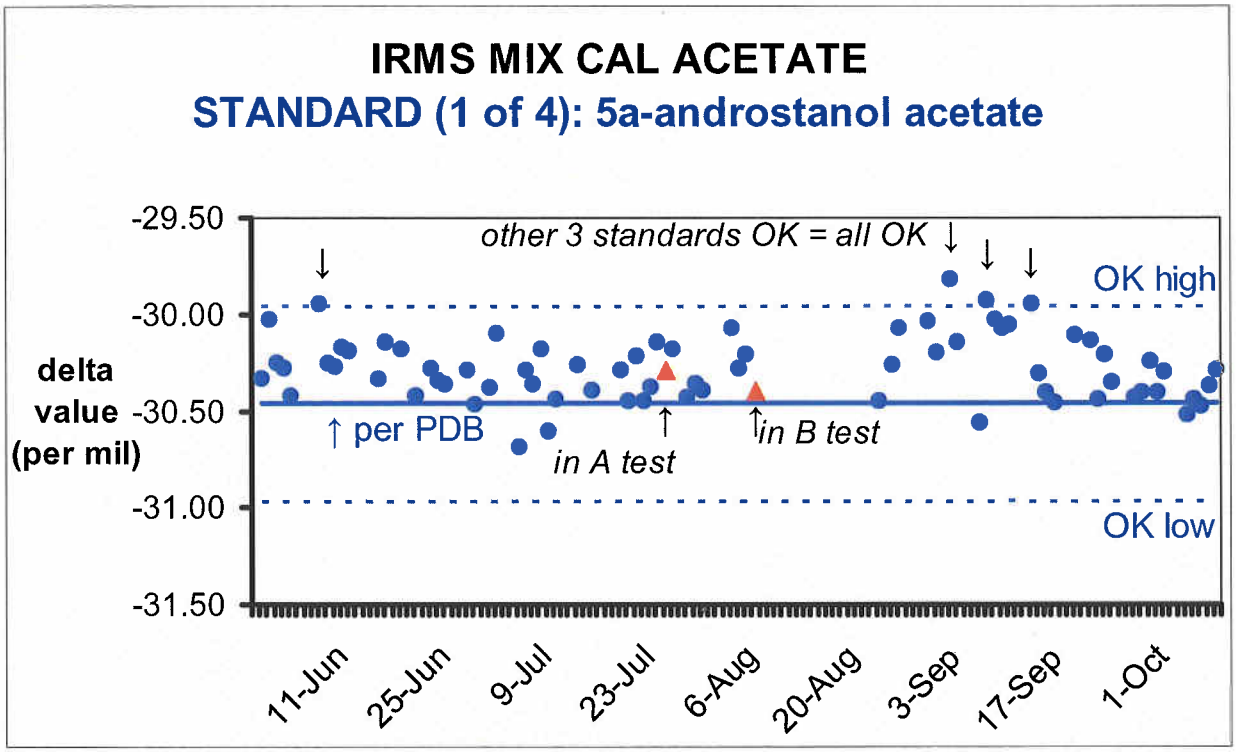


Figure 5



The Mix Cal Acetate results from the controls run immediately before and immediately after Respondent's A and B samples were not only consistent with each other and the verified values established by Eurofins, they are also consistent with all other results from this Mix Cal Acetate control batch for over 75 samples analyzed between May 29, 2006 through October 6, 2006 (Exhibit 26, pages LNDD 0448 through 0450)[6]. As illustrated in Figures 6, 7, 8 and 9 below, this is true for each of the four compounds found in LNDD's Mix Cal Acetate mix.

Figure 6



[6] The values at LNDD 0448-0450 represent the Mix Cal Acetate measurements before (not after) each of the 75 samples was analyzed.

Figure 7

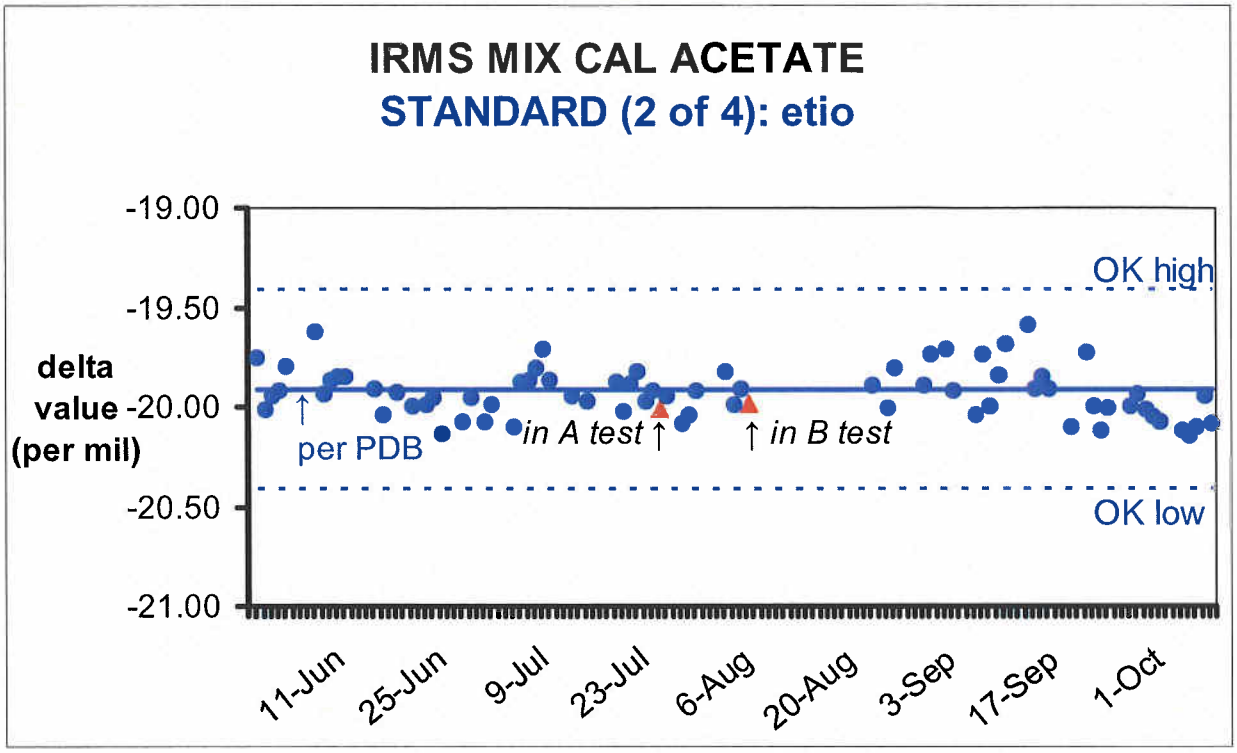


Figure 8

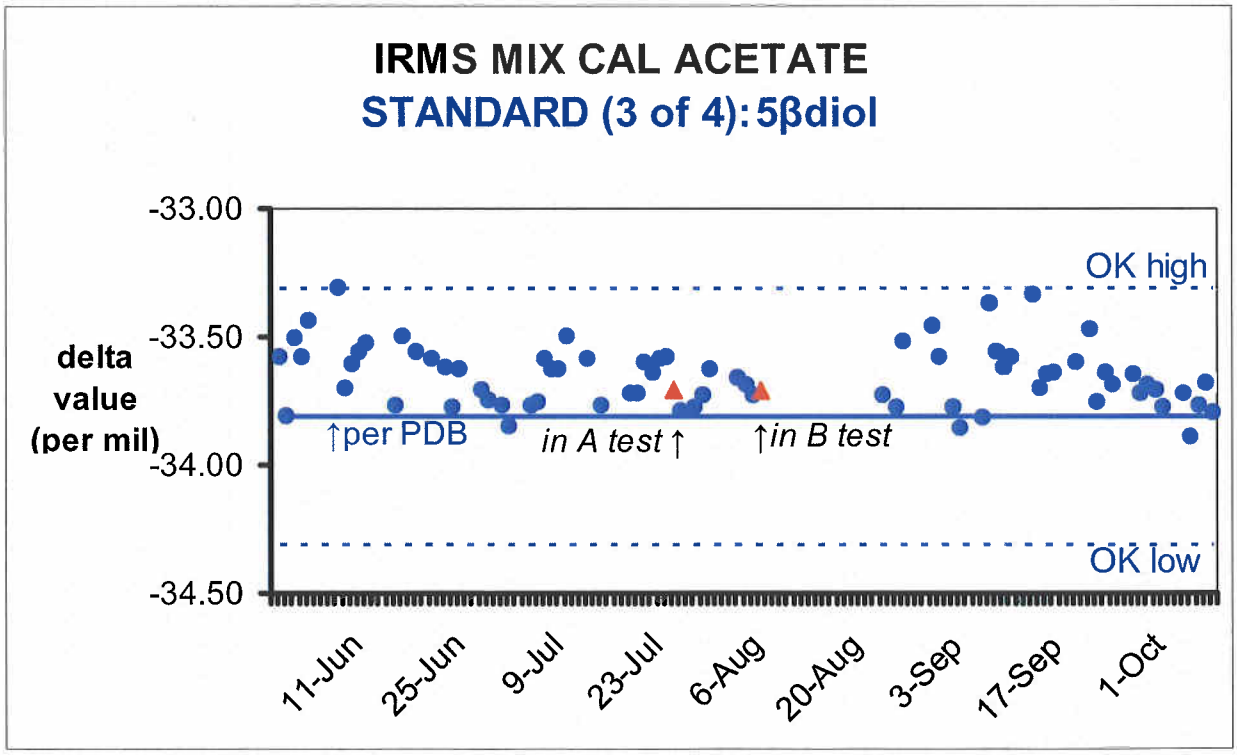
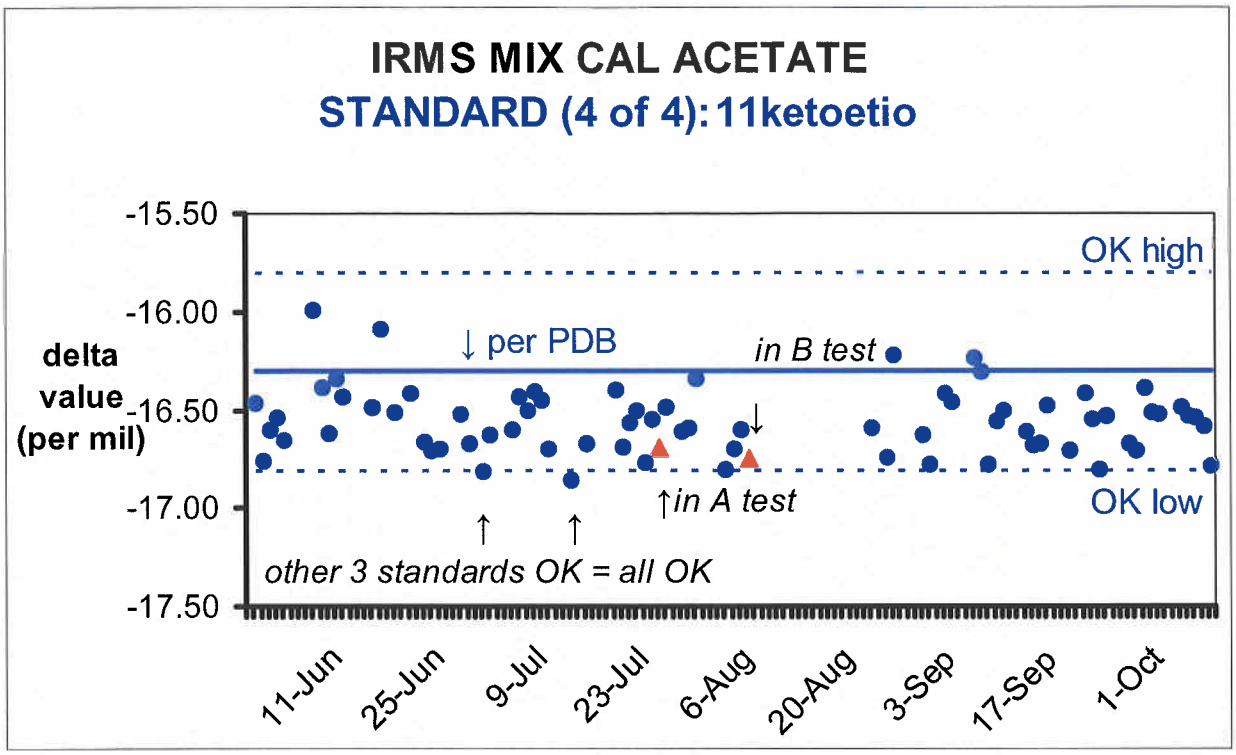


Figure 9



Each blue dot represents one of the 75 delta value determinations. The solid horizontal line represents the delta value measured by reference lab Eurofins against international standard PDB. The dashed horizontal lines represent the range of acceptability of the LNDD measurement on any day. The LNDD acceptability criterion is that on any day, at least three of four delta values (for at least three of the four standards present in the mix) must fall between the dashed lines. This criterion was met in every single analysis, including the A confirmation and the B confirmation for Sample #995474.

80. LNDD checked overall assay quality by injecting a Blank Urine ("Blu" in the injection sequence) from the same Blank Urine pool immediately before each of the three fractions of Respondent's urine was injected. The initial delta/delta value for each testosterone metabolite – endogenous reference compound – was calculated the first time the Blank Urine pool was analyzed (Exhibit 26, pages LNDD 0309-0310). Then with every subsequent IRMS

confirmation, one aliquot of Blank Urine in this pool was tested side-by-side with a sample. LNDD checks assay performance and the accuracy of each day's results by making sure that, of the four delta/delta values for the Blank Urine, at least three agree with LNDD's "initial" values. This is reflected in Figures 10 and 11 below.

Figure 10

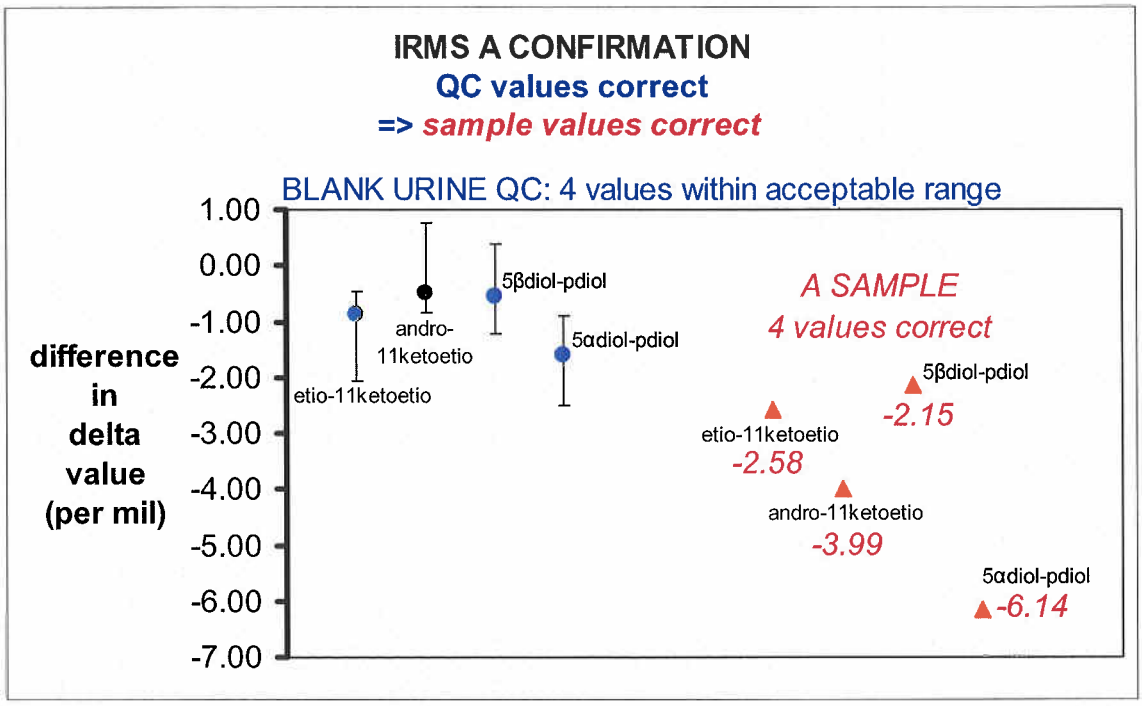
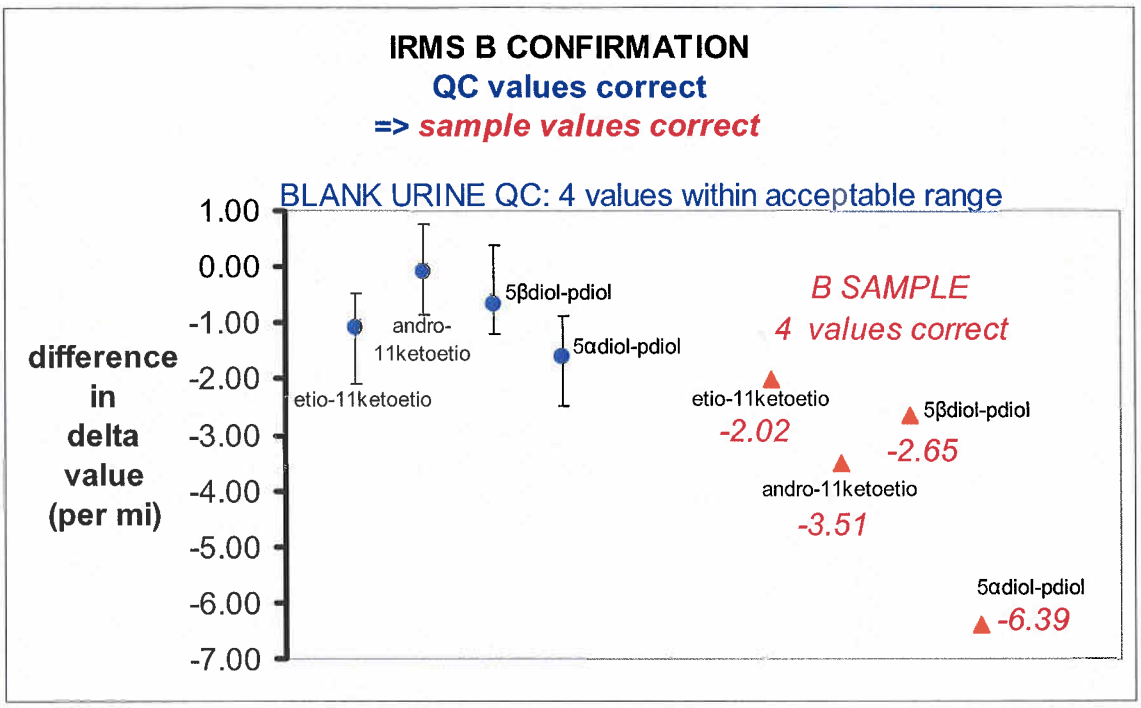


Figure 11



The vertical line through each dot is the range of acceptability of each measurement; it is equal to the "initial" difference in the delta/delta value measured by LNDD, ±0.8 delta/delta units. On any given day the criteria for acceptability is that at least three of the four dots must fall within the vertical line. This criteria was met on both the day of the IRMS A sample confirmation and the day of the IRMS B sample confirmation. Because the four delta/delta values are correct for the metabolites in the Blank Urine, then the delta/delta values for the same testosterone metabolites measured in Respondent's urine are also correct.

81. The delta/delta values for testosterone metabolites in the Blank Urines analyzed contemporaneously with Respondent's A and B samples were not only consistent with the "initial" values for that Blank Urine pool established by LNDD, they were also consistent with the results obtained each time an aliquot from that Blank Urine pool was used between June and August 2006. Figures 12, 13, 14 and 15 reflect the 43 times Blank Urines from this same Blank Urine pool were analyzed in the June through August period.

Figure 12

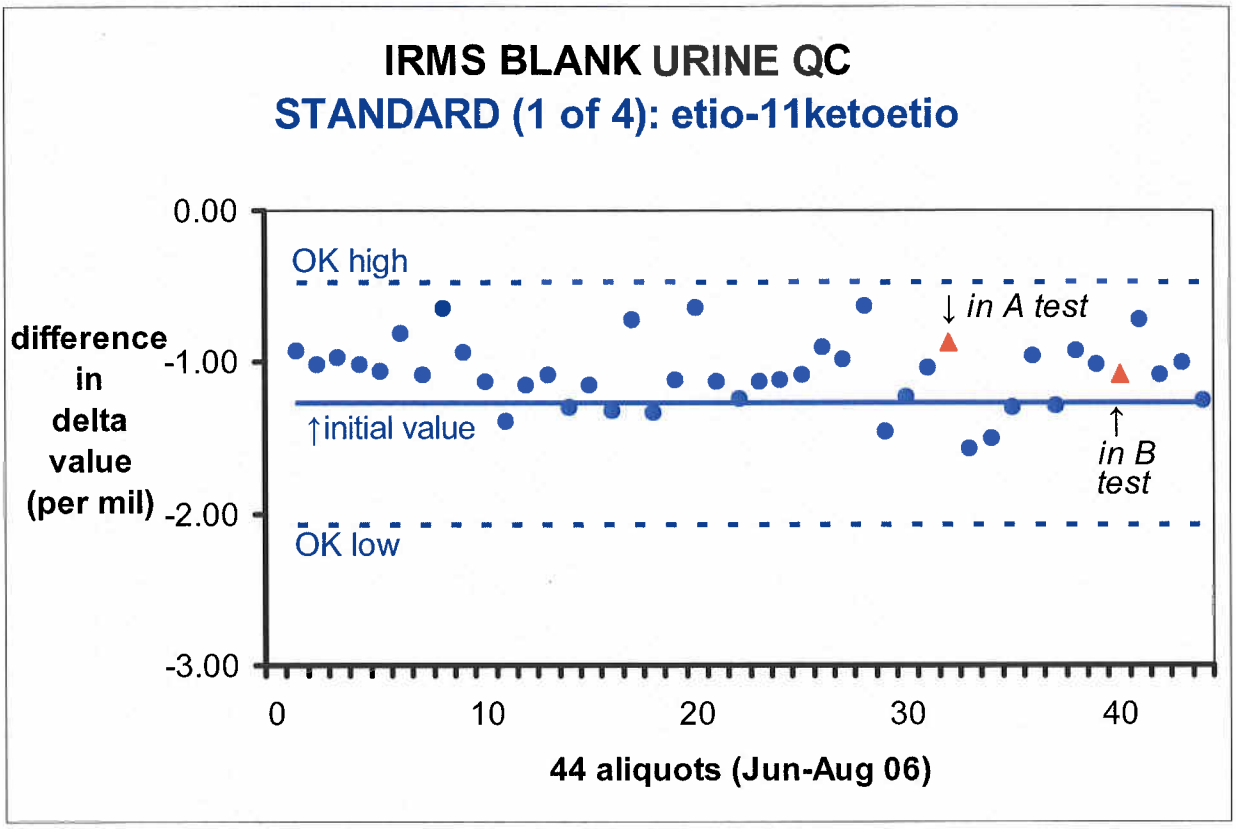

IRMS BLANK URINE QC
STANDARD (1 of 4): etio-11ketoetio
0.00
-1.00
-2.00
-3.00
difference in delta value (per mil)
OK high
OK low
initial value
in A test
in B test
0
10
20
30
40
44 aliquots (Jun-Aug 06)

Figure 13

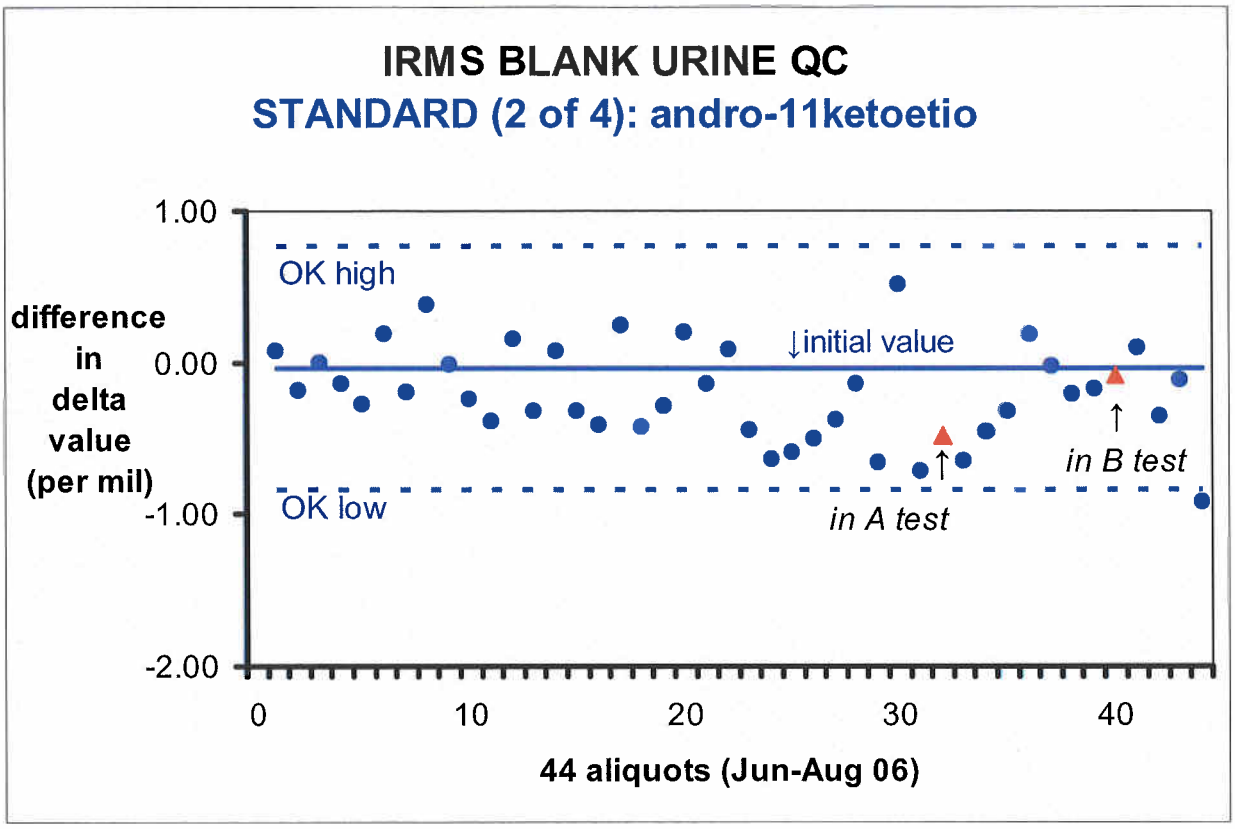

IRMS BLANK URINE QC
STANDARD (2 of 4): andro-11ketoetio
1.00
0.00
-1.00
-2.00
difference in delta value (per mil)
OK high
OK low
initial value
in A test
in B test
0
10
20
30
40
44 aliquots (Jun-Aug 06)

Figure 14

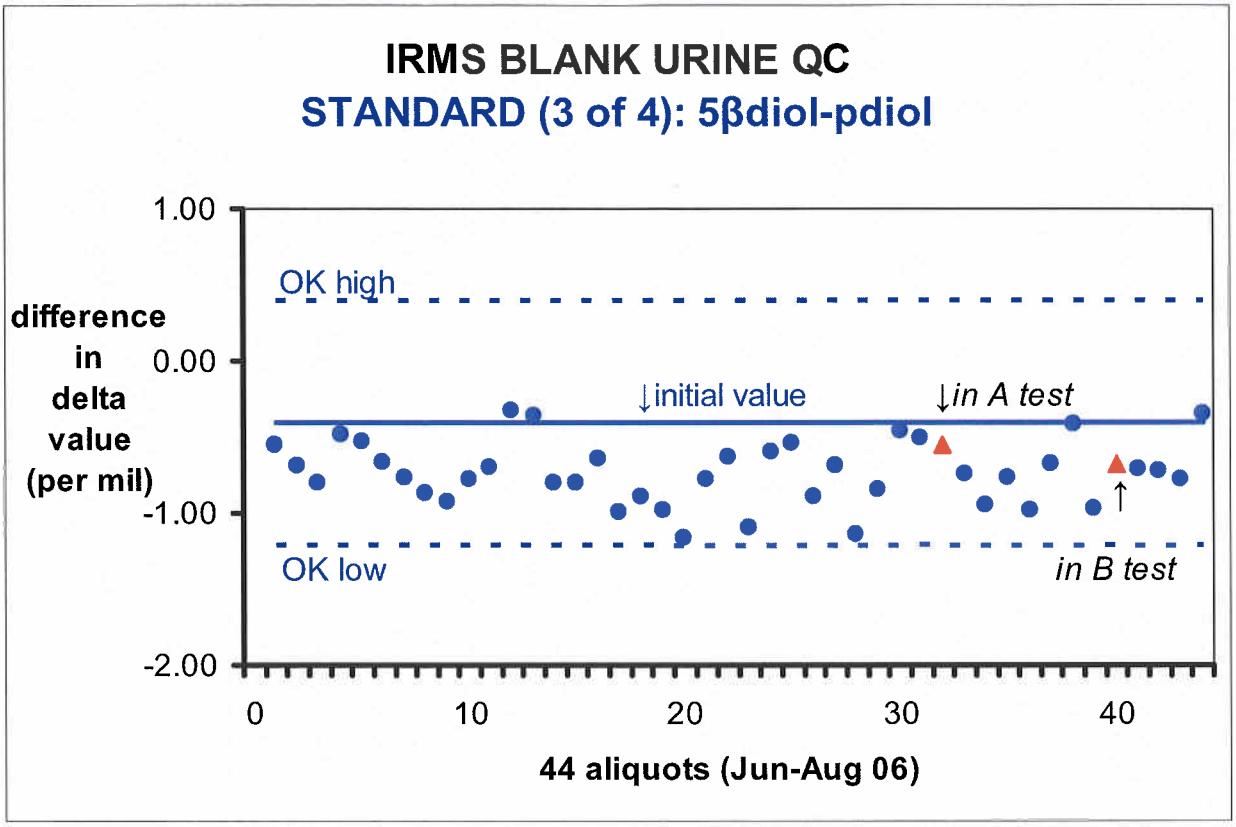
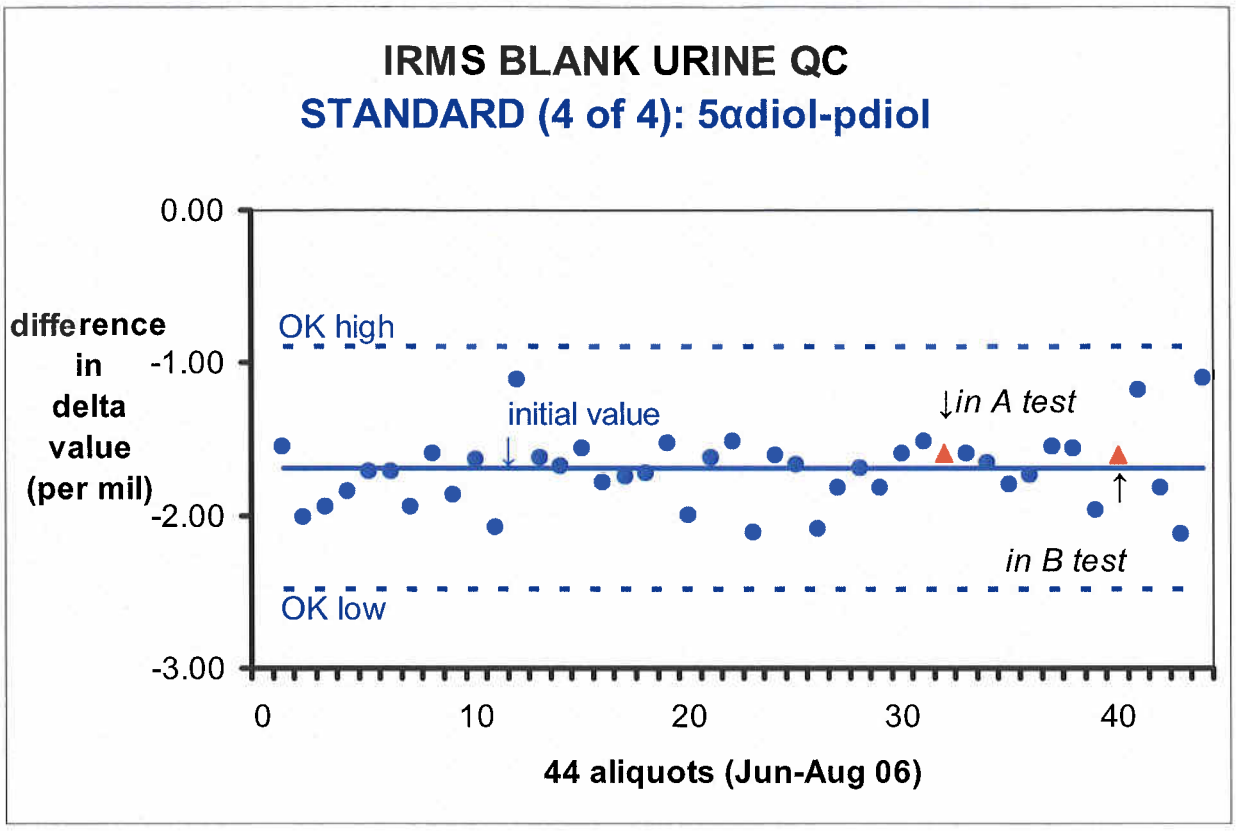

IRMS BLANK URINE QC
STANDARD (3 of 4): 5βdiol-pdiol
1.00
0.00
-1.00
-2.00
difference in delta value (per mil)
OK high
OK low
↓initial value
↓in A test
in B test
0
10
20
30
40
44 aliquots (Jun-Aug 06)

Figure 15



Each round dot on these Figures represents one of the 43 delta/delta measurements for that testosterone metabolite. The solid line represents the "initial" value measured by LNDD. The dashed horizontal lines represent the range of acceptability of the LNDD measurement on any day. The LNDD acceptability criteria is that on any day, every three of the four differences in delta values must fall between the dashed lines. This criteria was met in every single analysis, including the A confirmation and B confirmation for Sample #995474.

82. If the IRMS instrument had not functioned properly on the day of the A or B sample confirmation, at least one of the following would have been observed:

- no signals detected
- impossible to record any data
- failed verification of instrument performance, such as:

- failed tune
- failed stability check (i.e., CO_2 data widespread beyond acceptable range)
- failed precision check (i.e., Mix Cal IRMS outside acceptable range)
- failed accuracy check (i.e., Mix Cal Acetate delta values outside acceptable range)
- unacceptable Blank Urine data (i.e., delta/delta values outside acceptable range)

None of these failures were observed. Instead, eight different checks and controls on each day met acceptance criteria.

H. <u>The positivity criteria for IRMS analysis has been established by WADA.</u>

83. The World Code, accepted by UCI and the rest of the Olympic Movement, gives WADA the power to establish positivity criteria and other technical standards for the laboratories through the adoption of the ISL and Technical Documents.

> "*International Standards* for different technical and operational areas within the anti-doping program will be developed in consultation with the *Signatories* and governments and approved by *WADA*. The purpose of the *International Standards* is harmonization among *Anti-Doping Organizations* responsible for specific technical and operational parts of the anti-doping programs. Adherence to the *International Standards* is mandatory for compliance with the *Code*" (World Code, Introduction, page 2, Exhibit 4).
>
> "Once promulgated, Technical Documents become part of the *International Standard* for <u>Laboratories</u>" (International Standard for Laboratories, Article 1.0, page 5).
>
> "Compliance with an *International Standard* (as opposed to another alternative standard, practice or procedure) shall be sufficient to conclude that the procedures addressed by the *International Standard* were performed properly" (World Code Definition

of International Standard, page 74, Exhibit 4; UCI Rules, Exhibit 1, page 48).

84. WADA has established a positivity criteria for IRMS. That criteria is set forth in WADA Technical Document TD2004EAAS:

> **"3. Isotope ratio mass spectrometry:**
>
> "When a parameter of the steroid profile indicates a need to further study, its $^{13}C/^{12}C$ value expressed in delta units per mil (d ‰) or that of its metabolites will be measured and compared to that of urinary reference steroids within the sample not affected by administration. Depending upon the nature of the endogenous steroid suspected to have been administered, the metabolites analysed could be testosterone, epitestosterone, androsterone, etiocholanolone, the androstanediols, DHEA, or other relevant metabolites while the urinary reference steroid usually analysed by the Laboratories is one of, pregnanediol, pregnanetriol, cholesterol, 11-hydroxyandrosterone or 11-ketoetiocholanolone. The instrumentation should be calibrated with an appropriate Reference Material.
>
> "The results will be reported as consistent with the administration of a steroid when the $^{13}C/^{12}C$ value measured for the metabolite(s) differs significantly i.e. by 3 delta units or more from that of the urinary reference steroid chosen. In some *Samples*, the measure of the $^{13}C/^{12}C$ value of the urinary reference steroid(s) may not be possible due to their low concentration. The results of such analyses will be reported as 'inconclusive' unless the ratio measured for the metabolite(s) is below -28‰ based on non-derivatised steroid" (page 3, *emphasis added*).

Respondent acknowledges at page 8 of his Discovery Brief that this is "the positivity criteria mandated by WADA."

85. The difference between the value measured for the metabolites and the urinary reference steroids in Respondent's sample were as follows:

A Sample	B Sample
5 alpha diol -Pdiol: -6.14	5 alpha diol -Pdiol: -6.39
Andro -11ketoetio: -3.99	Andro -11ketoetio: -3.51
Etio -11ketoetio: -2.58	Etio -11ketoetio: -2.02
5 beta diol -Pdiol: -2.15	5 beta diol -Pdiol: -2.65

86. Respondent has contended that his sample is not positive under the WADA criteria because: (1) the measured differences for all of the metabolites in his urine were not at least -3 delta units; (2) LNDD did not properly consider uncertainty of measurement in reporting the stated values for Respondent's sample; and (3) some WADA-accredited laboratories use a positivity criteria as high as -4 delta/delta units instead of -3 delta/delta units. These arguments will each be addressed in the following sections.

I. A difference of -3 delta units in a single metabolite establishes doping under the WADA criteria.

87. Dr. Christiane Ayotte, the Director of the Montreal WADA-accredited laboratory, was the principal drafter for the WADA Working Group that prepared TD2004EAAS. Dr. Ayotte will testify that in drafting TD2004EAAS for WADA she attempted to make clear that a difference of -3 delta/delta units in a single metabolite was sufficient to establish positivity by using the term "metabolite(s)." If the intention had been to include the plural (all metabolites), the phrase would not have been written to include both the singular and the plural; it would have simply been written as "metabolites." Note that elsewhere in this section of the Technical Document when the plural is intended, the term "metabolites" is used.

88. Furthermore, from a scientific perspective, it is clear that individuals who dope with testosterone or its precursors may, depending on the prohibited substance, how it is administered, and when after administration the sample is taken, show a difference of at least -3 delta/delta units only in a single metabolite. The determination of which testosterone metabolite will be the most sensitive and long-lasting indicator of testosterone abuse is a function of many

variables. Those variables include metabolic differences amongst individuals, the particular prohibited substance taken, the route of administration, and the time after administration when the sample is collected. There is no question, however, that depending on this combination of factors, the difference in delta/delta values in the metabolites of someone who has used testosterone is not always uniform. Sometimes the delta/delta values of all of the metabolites are similar; other times the delta/delta values of two of the metabolites are increased; and in some other cases the delta/delta value of only one metabolite is significantly affected by testosterone administration. Several research studies clearly prove the point that in some cases doping can only be established with reference to the delta/delta value of a single metabolite.

a. UCLA Study. UCLA conducted a study in which testosterone was administered by injection to a healthy male volunteer over a three-day period. As described in Figure 16, the delta/delta values of that volunteer in two urine samples collected from 12 to 17 hours and from 17 to 25 hours after the end of testosterone administration were strikingly similar to the delta/delta values in Respondent's Sample #995474.

Figure 16

Delta/Delta	**Respondent**	**UCLA Subject**
5 alpha diol-Pdiol	A -6.14 B -6.39	12-17 hours* -7.0**[7] 17-25 hours* -5.1**
5 beta diol-Pdiol	A -2.15 B -2.65	12-17 hours* -2.3** 17-25 hours* -2.3**

* after end of T administration

[7] **To render UCLA data comparable to Respondent's data, first the UCLA delta values were corrected for acetate as follows:

- UCLA acetylation reagent delta value: -37.35 (Exhibit 36, Table 2 footnote)
- UCLA corrected 5αdiol and 5βdiol delta value = (measured delta * 23 + 4 * 37.35)/19
- UCLA corrected 5pdiol delta value = (measured delta * 25 + 4 * 37.35)/21
- then the delta/deltas were calculated based on the corrected deltas.

(See Exhibit 36.)

If, as Respondent suggests, delta/delta values of at least -3 or more are required for more than one metabolite, this UCLA volunteer, who had been receiving testosterone injections for three days, could not be declared positive.

b. Cologne Study. The Cologne laboratory conducted a study involving the administration of testosterone gel to 18 healthy males. One group of 9 volunteers received dermal application of testosterone gel daily for six weeks. The other group of 9 volunteers received dermal application of testosterone gel every other week for six weeks. The urine samples of three of these volunteers have been analyzed by IRMS. It is clear from this study that when testosterone gel is applied to the skin that there are significant differences in the delta/delta values of the various testosterone metabolites. Because the skin contains five alpha reductase enzymes which encourage the metabolism of testosterone along the five alpha diol pathway, the detection of dermal testosterone gel administration is much more likely to be achieved by measuring the delta/delta value of 5 alpha diol than the other testosterone metabolites.

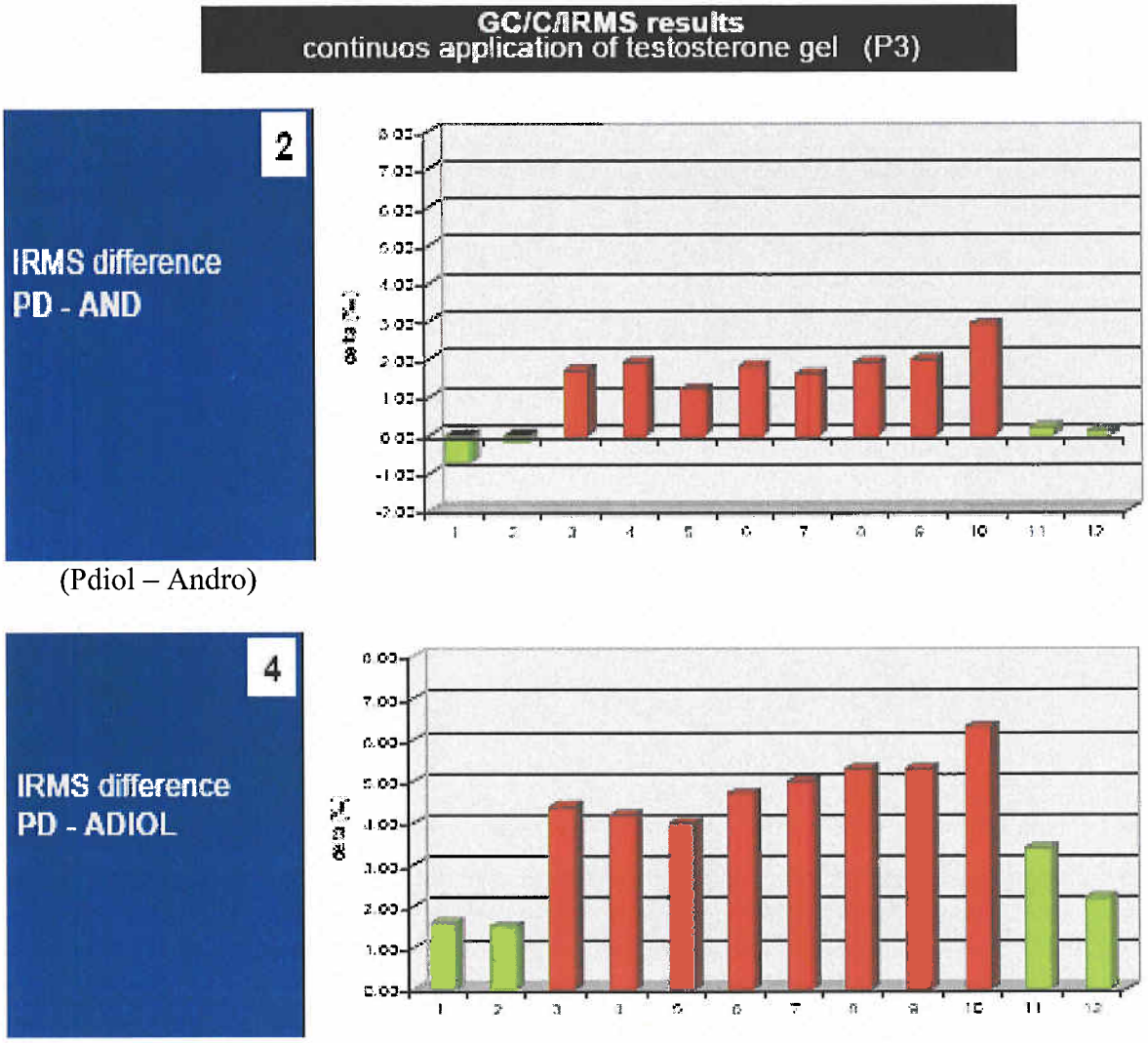
> "The results also indicate that after transdermal application the conversion of testosterone to Adiol is much stronger than the conversion to Bdiol ... The conversion of testosterone to 5-alpha-steroids after transdermal application is probably due to a high 5-alpha-reductase activity of the skin" (Exhibit 34, page 7).
>
> "The results of the GC/C/IRMS analyses show that for the detection of the misuse of T-gel the target compounds T and Adiol are much more suitable than And, Etio and Bdiol" (Exhibit 34, page 13).

The fact that, of the four testosterone metabolites measured by LNDD, 5 alpha diol may be the only one that can detect doping with testosterone gel is illustrated in Figures 17 and 18 which

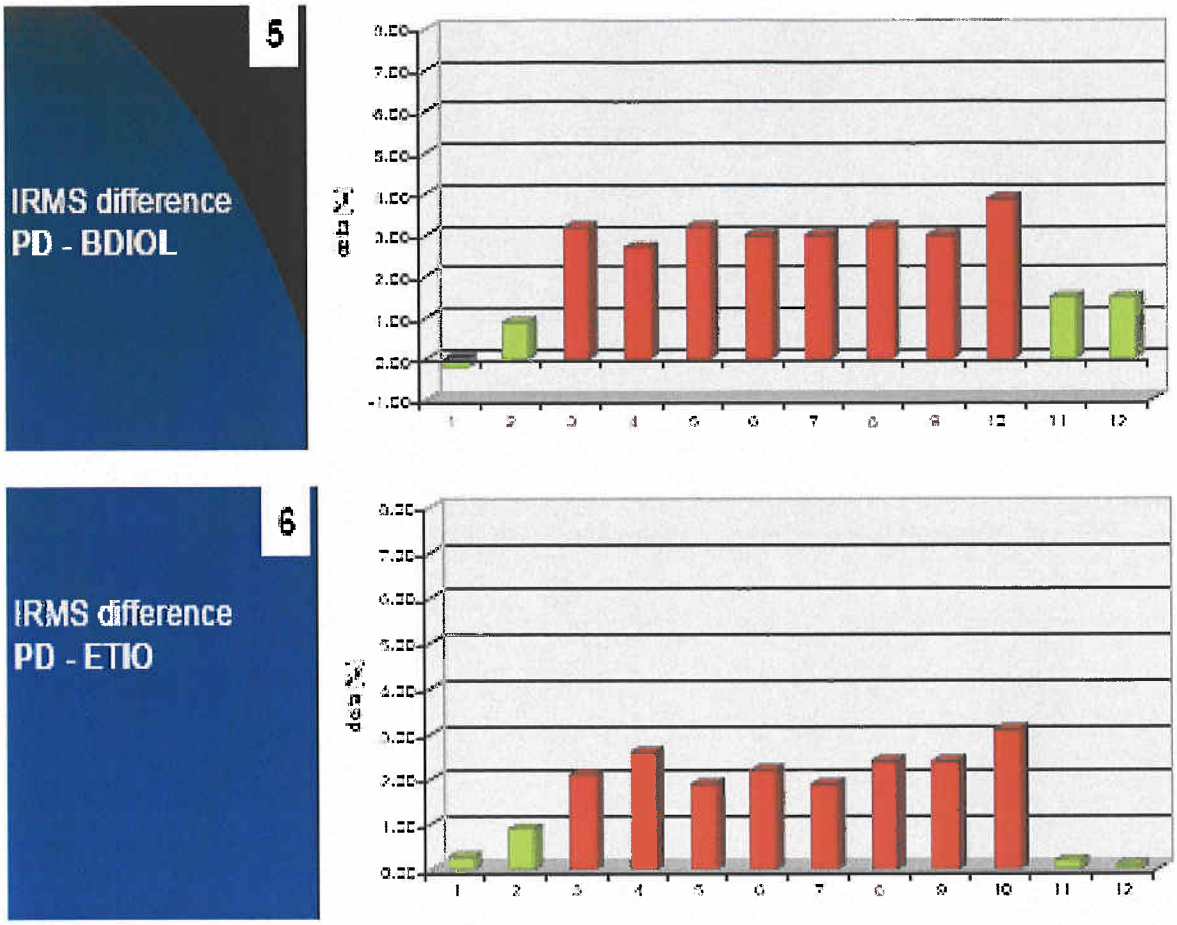
show the results for Volunteers P3 and P9 from the Cologne Study. Volunteer P3 received application of a testosterone gel daily for six weeks. Volunteer P9 received daily application of testosterone gel every other week for six weeks.

Figure 17

Volunteer P3

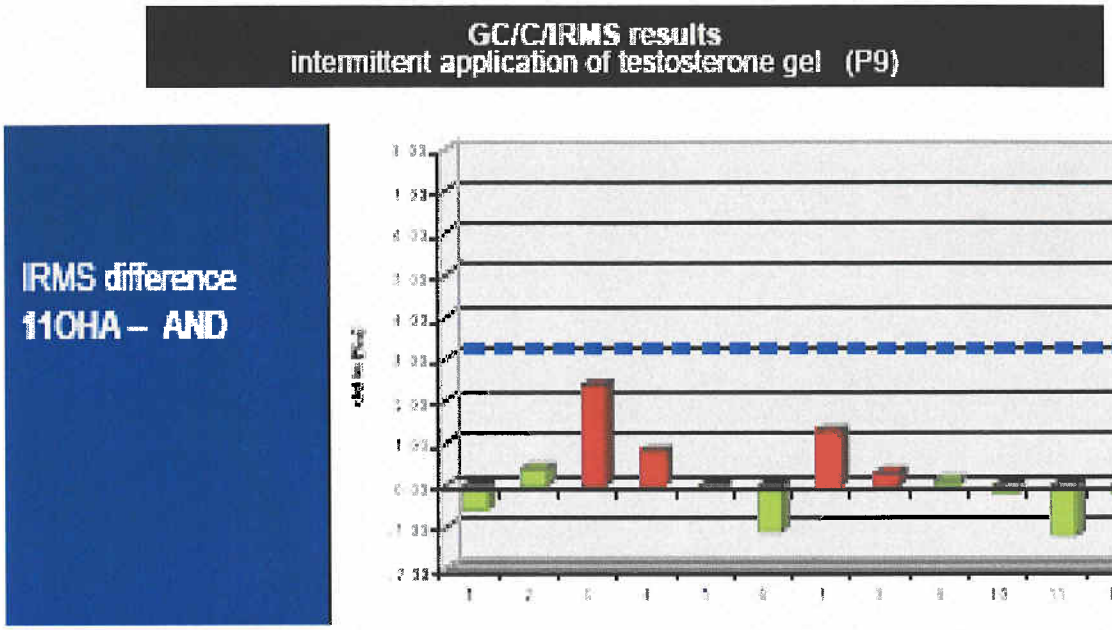


(Pdiol – Andro)

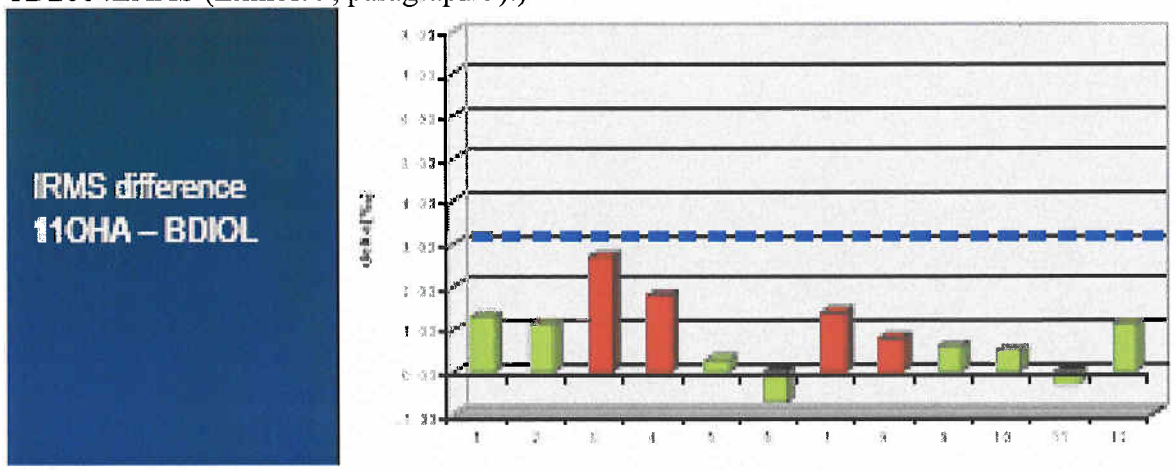


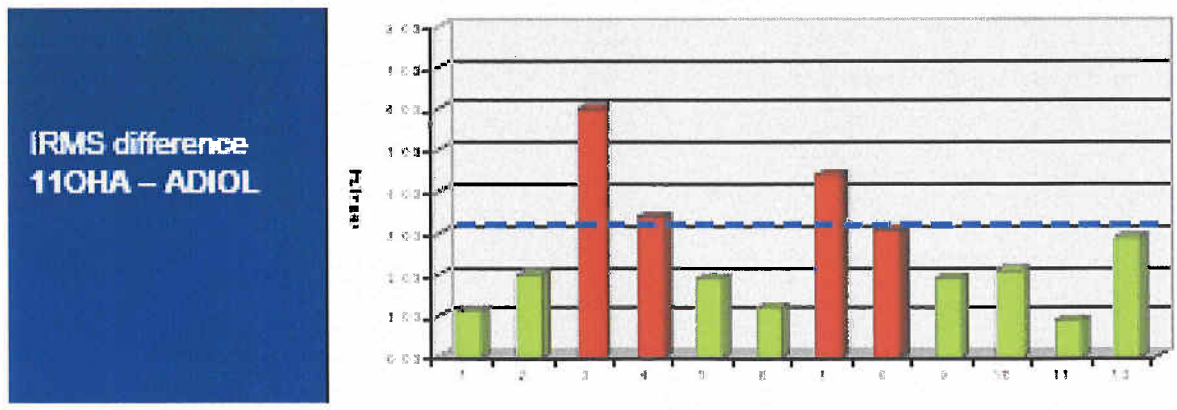
Note that in the middle of the administration period (6 and 7 on the bar graph), only the delta/delta value for 5 alpha diol exceeded -3 delta/delta units (Exhibit 34, pages 14 and 15).

Figure 18
Volunteer P9



(11OHA is one of the other endogenous reference compounds approved by WADA in TD2004EAAS (Exhibit 9, paragraph 3).)





Note that for Volunteer P9, 5 alpha diol is the only one of the four testosterone metabolites measured by LNDD that ever exceeded the WADA -3 delta/delta unit criteria. The protocol for the Cologne research project is found in Exhibit 34, pages 1 and 2). The data for Volunteer P3 is found at Exhibit 34a.

89. Montreal DHEA Research. The Montreal laboratory has done IRMS research on the administration of DHEA and androstenedione. One such study demonstrates that after the administration of DHEA or androstenedione the delta values of the different testosterone metabolites for two volunteers return to normal at very different rates (Exhibit 40 at USADA 1154, page 6).

J. The WADA positivity criteria of -3 delta units does not anticipate that the measured delta/delta value obtained by the laboratory will be reduced by a factor for measurement uncertainty.

90. In its conclusions stating that IRMS analysis established the use of exogenous testosterone or its precursors, LNDD reported the difference in delta values between andro -11ketoetio and 5 alpha diol -Pdiol without any adjustment for measurement uncertainty.

> "L'analyse par spectrométrie de masse de rapport isotopique indique une origine exogène des métabolites de la testostérone, cohérente avec une prise de testostérone ou de l'un de ses précurseurs. L'origine exogène des métabolites de la testostérone a été objectivée sur la base d'un appauvrissement isotopique de 3.51‰ et -6.39‰ respectivement pour les métabolites androstérone et 5 α androstanediol" (USADA page 0352, Exhibit 25).
>
> "Isotope Ratio Mass Spectrometry analysis indicates an exogenous origin for the metabolites of testosterone, consistent with the administration of testosterone or one of its precursors. The exogenous origin of the metabolites of testosterone was revealed by an isotopic depletion of 3.51‰ and -6.39‰, respectively, for the following metabolites: androsterone and 5α-androstanediol" (English translation of USADA page 0352).

In a table of values found in the same reports, LNDD shows that if an uncertainty factor were to have been applied to its IRMS delta/delta results, that uncertainty factor would be $\pm$0.8 delta/delta units (Exhibit 24, USADA page 0186 and USADA page 0352). LNDD's $\pm$0.8 uncertainty factor for delta/delta measurement was certified by ISO as part of ISO's 2006 certification of LNDD (Exhibit 26, page 0098).

91. Under the ISL and the applicable Technical Documents, LNDD's statement in its conclusion was correct because LNDD was not required to take into account uncertainty in the measurement of IRMS delta values. The ISL addresses the issue of uncertainty at Article 5.4.4.3 which provides as follows:

> "5.4.4.3 Estimate of Uncertainty of Method
> In most cases an identification of a *Prohibited Substance*, its *Metabolite(s)* or *Marker(s),* is sufficient to report an *Adverse Analytical Finding*. Thus, quantitative uncertainty as defined in ISO/IEC 17025 does not apply. In the identification of a compound by GC/MS or HPLC/MS, there are qualitative measures that substantially decrease the uncertainty of identification.
>
> "In the case of a Threshold Substance, uncertainty in both the identification and the finding that the substance is present in an amount greater than the threshold concentration must be addressed" (page 34, Exhibit 8).

It is clear from the ISL that uncertainty need only be addressed in the case of a Threshold Substance. "Threshold Substance" is a defined term in the ISL:

> "Threshold Substance: A substance listed in the *Prohibited List* for which the detection of an amount in excess of a stated threshold is considered an *Adverse Analytical Finding*" (page 11, Exhibit 8).

Exogenous testosterone as measured by isotopic ratio delta/delta units is not listed in any WADA document as a Threshold Substance. To the contrary, the WADA Prohibited List states, "In all cases, and at any concentration, the *Athlete's* sample will be deemed to contain a *Prohibited Substance* and the laboratory will report an *Adverse Analytical Finding* if, based on any reliable analytical method (e.g., IRMS), the laboratory can show that the *Prohibited Substance* is of exogenous origin" (Exhibit 5, page 3). The reference to "and at any concentration" makes clear that exogenous testosterone measured by IRMS is not a Threshold Substance. Similarly, in WADA Technical Document TD2004MRPL, which expressly lists the nine WADA Threshold Substances, no reference is made to isotopic ratio delta values or exogenous testosterone (Exhibit 10, page 2).

92. In the Landaluce case Respondent's expert, Dr. de Boer, contended that the difference in delta values obtained by LNDD's IRMS analysis should have been adjusted for uncertainty and that the proper measure of uncertainty for LNDD's IRMS method comparing a metabolite to an endogenous reference compound should be 1.35 delta/delta units instead of 0.8 delta/delta units as stated in the LNDD documents (Exhibit 22, paragraph 73). In Landaluce, UCI and its expert Dr. Saugy, the Director of the Lausanne laboratory, contended that since testosterone as measured by IRMS is not a Threshold Substance, no adjustment to the measured value should be made for uncertainty. The Panel noted the disagreement between the experts and concluded that Mr. Landaluce had not succeeded in reversing the presumption that LNDD's analysis was in compliance with the uncertainty requirements of the ISL (Exhibit 22, paragraphs 72-79).

K. Respondent's sample would also be positive under the criteria in effect before TD2004EAAS.

93. Before WADA Technical Document TD2004EAAS became effective on 13 August 2004, those WADA-accredited laboratories performing IRMS analysis applied one of two types of positivity criteria. LNDD and several other laboratories used the ratio of the delta value of a metabolite over the delta value of an endogenous reference compound. The ratio used by LNDD was 1.12. This ratio is referenced in the studies found at Exhibit 26, pages LNDD 0208-0218. Similar ratios were regularly discussed in the scientific literature. (See "Confirming testosterone administration by isotope ratio mass spectrometric analysis of urinary androstenediols," Exhibit 40, USADA 1241, page 383.) At LNDD, samples having a ratio greater than 1.12 were declared positive. Respondent's sample would clearly have been declared positive under the 1.12 ratio criteria.

	USADA page number	5αdiol delta value (per mil)	Pdiol delta value (per mil)	**5αdiol delta/ pdiol delta**	**>1.12?**
A sample	0185	-27.72	-21.58	**1.28**	**YES**
B sample	0351	-27.43	-21.05	**1.30**	**YES**

	USADA page number	5βdiol delta value (per mil)	Pdiol delta value (per mil)	**5βdiol delta/ pdiol delta**	**>1.12?**
A sample	0185	-23.73	-21.58	1.09	no
B sample	0351	-23.69	-21.05	**1.12(5)**	**YES**

	USADA page number	andro delta value (per mil)	11 ketoetio delta value (per mil)	**andro delta/ 11 ketoetio delta**	**>1.12?**
A sample	0185	-25.05	-21.06	**1.18**	**YES**
B sample	0351	-25.29	-21.78	**1.16**	**YES**

The ratio of 1.12 was also used by the Montreal laboratory. The findings of a ratio of delta values greater than this positivity criteria was the basis of the Montreal laboratory's declaration

of exogenous testosterone use in the Dos Santos case. The ratios reported by Montreal in Dos Santos were even lower (less positive) than Respondent's ratios (Exhibit 15, paragraph 11).

94. Other WADA-accredited laboratories, such as UCLA, Cologne and Sydney, followed the current WADA approach by basing their finding of positivity on the difference between the delta value measured for a metabolite and the delta value measured for a urinary reference standard. Depending on the particular metabolite and endogenous reference compound being compared, the positivity criteria used by these laboratories has ranged from -3 delta/delta units to -4 delta/delta units. In all cases measurement uncertainty has been incorporated into the established delta/delta positivity criteria and the laboratory's analytical result for a particular sample was not further reduced for uncertainty. Whether the applicable positivity criteria is -3 delta/delta units or -4 delta/delta units makes little difference in this case since a difference of more than -6 delta/delta units was found for 5 alpha diol -Pdiol in Respondent's sample.

L. Respondent's sample is positive by any criteria.

95. The difference in delta/delta values between 5 alpha diol –Pdiol in Respondent's A and B samples was -6.14 and -6.39 respectively. These are very high delta/delta values. Respondent's sample is still positive even using all contested assumptions which are most favorable to the Respondent. For example:

a. Use -4 delta/delta units instead of the -3 delta/delta units specified in the WADA criteria.

b. Adjust the values measured by LNDD for uncertainty (even though the laboratories that would use -4 delta/delta units as a criteria have already taken uncertainty into account in arriving at the -4 delta/delta figure).

c. Instead of the .08 delta/delta unit measure of uncertainty determined by LNDD in its validation testing, use Dr. de Boer's testimony in Landaluce that the correct measure of uncertainty for LNDD's delta/delta measurements should be 1.35 delta/delta units.

The extreme approach of cumulating arguments (a) – (c) above would require that the difference between Respondent's 5 alpha diol -Pdiol be at least 5.35 delta/delta units. In fact, the difference in both Respondent's A and B samples was greater than -6 delta/delta units.

M. Respondent's defenses allegedly pertaining to LNDD's IRMS analysis fail to demonstrate any violation of the ISL by LNDD.

96. Based on Respondent's extensive media campaign and Respondent's Discovery Brief filed in this proceeding, USADA is able to anticipate a number of Respondent's alleged defenses. Most of these defenses go to the T/E ratio analysis performed by LNDD on Sample #995474, not the analysis of that sample using IRMS. T/E ratio-related defenses will be addressed separately in Section V of this brief. Because, as the CAS decisions have consistently stated, IRMS is a separate independent method for establishing the use of exogenous testosterone, the alleged defenses to LNDD's T/E ratio analysis are not relevant to the validity of its IRMS findings. Those alleged defenses of Respondent which appear to pertain to LNDD's IRMS findings are discussed separately below.

97. Note that as discussed in Section II.B of this brief, only those complaints by Respondent that rise to the level of violations of the ISL can justify rebutting the presumption that the laboratory analysis was performed properly.

N. Respondent's allegation: "LNDD's use of outdated GC/IRMS software."

98. The "Isoprime" IRMS instrument used by LNDD and the operating software for that instrument were sold to LNDD by a British company, MicroMass, in October

1998. Both the Isoprime instrument and the accompanying software were developed by MicroMass. MicroMass installed the Isoprime instrument at LNDD and provided training for the LNDD staff at the time of installation. Since installation LNDD has had continuing service from MicroMass or its successor GV Instruments. Never during this entire period did MicroMass or GVI tell LNDD that the software provided was not suitable for the Isoprime instrument or that it should have been upgraded. Like LNDD, laboratories around the world continue to successfully use the Isoprime instrument with its original software package.

99. It is erroneous for Respondent to assert that the Optima GC1.67-2 software is not suitable for use on the Isoprime instrument. Indeed, the Isoprime instrument was designed to be compatible with the existing Optima GC1.67-2 software. It is also clear from the Isoprime user manual produced by Respondent that the software provided is compatible for use on both the Isoprime and Optima instruments with certain functions available for the Optima instrument which are not used on the Isoprime instrument (see e.g., Exhibit 48).

100. Respondent is also incorrect in asserting that ISO document 17025 required LNDD to update the software which MicroMass provided with the instrument. Respondent's reference to the ISO requirement in its discovery brief is clearly misleading. Respondent states at page 17, "International Standard ISO/EC17025.5.5.11(2005) requires that 'where calibrations give rise to a set of correction factors, the laboratory shall have procedures to ensure that copies (e.g., computer software) are correctly updated.'" The Respondent's claim is that this ISO provision required LNDD to update the MicroMass software. In fact, Respondent left out a critical word in quoting ISO Section 5.5.11. What 5.5.11 actually says is:

> "5.5.11 Where calibrations give rise to a set of correction factors, the laboratory shall have procedures to ensure that copies (e.g., **in** computer

> software) are correctly updated" (Exhibit 23, *emphasis added*).

ISO Section 5.5.11 does not require that a user continually purchase updates in computer software; rather, it requires that when correction factors are based on the laboratory's most recent calibration, those correction factors should be included in all of the laboratory's files, including its computer software. Respondent's reference to ISO Section 5.5.4.7.2 is also not applicable because the Section expressly refers to computer software "developed by the user." In this case LNDD is the user and the computer software at issue was developed, not by LNDD, but by MicroMass (see Exhibit 23, page 15).

101. As a matter of further clarification, Respondent's reference to ISO 17025 as an "international standard" is also misleading. ISO 17025 is not an "International Standard" as that term is used in the World Code or UCI rules.

102. Respondent's allegation that LNDD's use of the original Optima GC1.67-2 software somehow violates ISO requirements is entirely undercut by the fact that LNDD's IRMS method was specifically included in its ISO certification.

EC31	Urine	Détermination de l'origine des métabolites et précurseurs de la testostérone par CG/C/IRMS CD : $\delta^{13}C$	Extraction SPE Dérivation Ac_2O/Pyridine Analyse IRMS	Isoprime Micromass Extractions : Cartouche C18/ 1-MeOH 2- CH_3CN 3-H_2O/ CH_3CN (F1-F2) CH_3CN (F3) Colonne : DB17MS (35m-0.25mm-0.25µm)	EC31-VA1 I-CONF-31 : M-Ex-24 M-An-41	Variation maximale admissible = 0,5‰

(Exhibit 26, LNDD page 0098)

103. Further, it is unlikely that any of the software upgrades referenced in Respondent's document production brief would have any impact on the reliability or accuracy of the instrument. Indeed, most of the upgrades references by Respondent are simply convenience items.

104. Finally, contrary to Respondent's speculation concerning how the Isoprime instrument might have performed better had different software been used, LNDD has provided hard analytical data from multiple controls analyzed contemporaneously with Respondent's sample which establish that the results produced by the Isoprime instrument on the days Respondent's A and B samples were analyzed were very precise and accurate. This control data has previously been discussed in Section IV.G.

O. <u>Respondent's allegation: "LNDD's GC/IRMS instrument was improperly used and maintained.</u>

105. Respondent claims that during the A sample analysis the IRMS instrument was operated at an improper pressure (5.2E-6mBar) which theoretically could have caused inaccurate results. This allegation is based on a statement in the Isoprime user manual instructing the user to ensure that the Penning gauge reading is less than 5E-6mBar.

106. Contrary to the statement in the user manual, MicroMass and GVI engineers consistently told LNDD during training that pressures lower than 6E-6mBar were appropriate for operation of the instrument. This instruction is consistent with the operational parameters of the instrument itself. The instrument has a built-in operating light which establishes that the instrument is operating within the correct pressure range. When the instrument is operating properly a green light is displayed on the instrument. If the operating pressure becomes too high, the light turns yellow as a warning followed by red and instrument shutdown. Exhibit 32 is three color photographs of the LNDD Isoprime instrument operating at a pressure of 5E-6mBar with the green light displayed.

107. Respondent's speculation that the values measured by the Isoprime instrument during Respondent's A sample analysis might be inaccurate because of operating pressure is laid to rest by the demonstrated precision and accuracy of the various controls that

were run on the instrument contemporaneously with Respondent's A sample. This demonstrated precision and accuracy was discussed in detail in Sections IV.G. Respondent's speculation is also laid to rest by the fact that results of Respondent's B sample, and the controls run in conjunction with that sample, were virtually identical to the A sample results even though the operating pressure of the instrument during the B sample analysis was 2.8E-6mBar. Whether the pressure was 2.8E-6mBar (B sample) or 5.2E-6mBar (A sample), the fact that the same results were obtained for the controls and Respondent's A and B samples on the two days regardless of analyzer pressure clearly demonstrates that Respondent's speculation that operating pressure might have distorted the A sample results is unfounded.

P. Respondent's allegation: "LNDD's laboratory documentation is riddled with errors."

108. Respondent's Exhibit 49 is a compilation of alleged LNDD documentation errors.

109. Almost all of these alleged documentation errors refer to documents from LNDD's T/E ratio analysis. In this regard, it is important to remember that CAS has held that an IRMS determination of exogenous testosterone is independent of any problems which may have arisen during T/E analysis. The alleged documentation errors in T/E ratio documentation will be discussed separately in Section V.F dealing with LNDD's T/E ratio analysis.

110. Exhibit 49 claims that there are nine errors in LNDD's IRMS documentation. LNDD's response to each of these claimed errors is summarized at Exhibit 32a. Nothing in Respondent's Exhibit 49 identifies a violation of the ISL or even casts the slightest doubt on the reliability of LNDD's IRMS results.

Q. Respondent's allegation: "The Landaluce/same operator error."

111. Article 5.2.4.3.2.2 of the ISL provides, "The 'B' *Sample* confirmation must be performed in the same laboratory as the 'A' *Sample* confirmation. A different analyst must perform the 'B' analytical procedure. The same individual(s) that performed the 'A' analysis may perform instrumental set up and performance checks and verify results."

112. In the Landaluce case the Panel found that LNDD had not complied with this requirement because all of the experts agreed, including Dr. de Ceaurriz, Director of LNDD, that there was a 10% overlap between the persons performing analytical procedures on the A and B samples (Exhibit 22, paragraph 102).

113. Once Mr. Landaluce established this departure from the ISL, under UCI Rule 19, the burden shifted back to UCI to establish that this departure had not caused the adverse analytical finding. The Panel noted that UCI did nothing to demonstrate that the departure from the ISL was not the origin of the adverse analytical finding other than to merely indicate in its appeal brief that, "And even if there had been a departure – quod non – this couldn't have led to the adverse analytical finding, unless it established that [the analyst] committed an error which caused the adverse analytical finding, quod non" (Exhibit 22, paragraph 105).

114. Respondent claims in his Discovery Brief that Cynthia Mongongu and Esther Cerpolini were both involved in performing analytical procedures on Respondent's A sample (which is true) and may have been involved in performing analytical procedures on Respondent's B sample (which is not true). The Panel will recall that these are the two women whose names appeared in the world press as having allegedly violated WADA requirements after Respondent failed to observe the Panel's initial confidentiality order.

115. Esther Cerpolini's involvement with the A sample was as the analyst for the first attempt at T/E confirmation, which was rejected. In the second attempt at T/E A confirmation, her only role was to correct page USADA 0079 (Exhibit 24) by initialing the pH and specific gravity values because they had been determined by her, and to verify the results. She had no role in the only analytical procedure that is relevant: the second T/E A confirmation. For the B sample, Ms. Cerpolini retrieved the intact, sealed B sample from the freezer. All Respondent's witnesses had the opportunity to observe this. She calculated the specific-gravity-based correction factor as seen on page USADA 0288 (Exhibit 25), a paperwork task not involving touching the sample. She also verified the results. None of these actions involved performing the B sample analytical procedure.

116. Cynthia Mongongu's involvement with the A sample was as the analyst for the IRMS confirmation. For the B sample she was a witness at the B sample opening (like Respondent's expert and lawyers) and she acted as verifying scientist while analyst Claire Frelat did sample preparation and instrumental analysis. This role is specifically permitted by the ISL.

117. Neither Ms. Cerpolini nor Ms. Mongongu did any of the following:

- Break the seal on the B bottle.
- Open the B bottle.
- Measure pH or specific gravity on the B sample.
- Aliquot the B sample for T/E or IRMS confirmation or any other purpose.
- Do any sample preparation on the B sample.
- Do any instrumental analysis on the B sample.
- Handle the B sample itself or any aliquot of the B sample after the B sample was opened.

In other words, neither woman performed any part of the analytical procedure on the B sample. Therefore, there was no departure from the WADA ISL Article 5.2.4.3.2.2.

R. Respondent's allegation: "The evidence of contamination/degradation of the sample."

118. As will be further discussed in Section V.D addressing Respondent's challenges to the T/E ratio analysis, there is no legitimate evidence that Sample #995474 was degraded. However, even if sample degradation occurred, it would not affect isotope ratio measurement. There have been two CAS cases in which Panels have held that even though the T/E ratio analysis had been compromised by potential sample degradation, that sample degradation would have no effect on the integrity of the results of IRMS analysis. For example, in Susin v. FINA the Panel concluded "the evidence on record firmly establishes that IRMS analysis is not affected by degradation ... the Panel is convinced that any degradation which may have occurred did not cause, or in any way qualify or mitigate, the positive results of the IRMS analysis" (Exhibit 14, paragraph 164). (See also WADA v. Wium, Exhibit 16, paragraph 6.7). This conclusion is also supported by the applicable research. For example, in a study entitled, "Validity of Carbon Isotope Ratio Measurements for Decomposed Urine Samples," the Sydney laboratory found that even with significantly deteriorated samples, IRMS delta values were not affected (Exhibit 40 at USADA 1216).

S. Respondent's allegation: "Laboratory blinding was a sham."

119. In his Discovery Brief, Respondent suggests that LNDD may have received a copy of Respondent's Doping Control Form with Respondent's name on it. That is simply not true.

120. After Respondent's sample was collected, Dr. Bordaberry and Dr. Tonelaere placed the laboratory's copy of the Doping Control Form (pink copy) in the cooler

with Respondent's sample to be shipped to the laboratory. Samples and laboratory copies of the Doping Control Forms for other riders whose samples were collected that day were also placed in the cooler. The French Anti-Doping Agency's (then CPLD, now AFLD) white copy of the form which contained Respondent's name and address was mailed by Dr. Bordaberry and Dr. Tonelaere, along with the white copies of the Doping Control Forms for other riders, to the CPLD. The CPLD copy of Respondent's Doping Control Form was received by CPLD on 27 July 2006 (Exhibit 27). Respondent is simply wrong in suggesting that this document was received by CPLD from the laboratory. LNDD never had the white copy of Respondent's Doping Control Form. Indeed, it is evident that the white copies of the Doping Control Forms for all of the Tour samples collected on July 20 were received in the mail together since all of them were stamped received by CPLD on 27 July 2006 (Exhibit 27a). The delay from sample collection to receipt at CPLD was a function of the French mail system. For example, the samples that were collected on the 19th of July were not received at CPLD until 28 July 2006 (Exhibit 27b).

121. Respondent also suggests that because of his success during the Tour, his well-known hip injury and his declaration of medications which is included on the laboratory's pink copy of the Doping Control Form, that laboratory personnel could have deduced his identity. This is pure speculation. Nothing that Respondent alleges is any violation of WADA's International Standards. Indeed, the WADA International Standard for Testing requires that an athlete provide a list of medications taken which is included on that part of the Doping Control Form that is sent to the laboratory. Most Doping Control Forms received by WADA-accredited laboratories contain lists of medications taken by the athlete. There is nothing particularly unique about the medications disclosed by Respondent which would establish his identity.

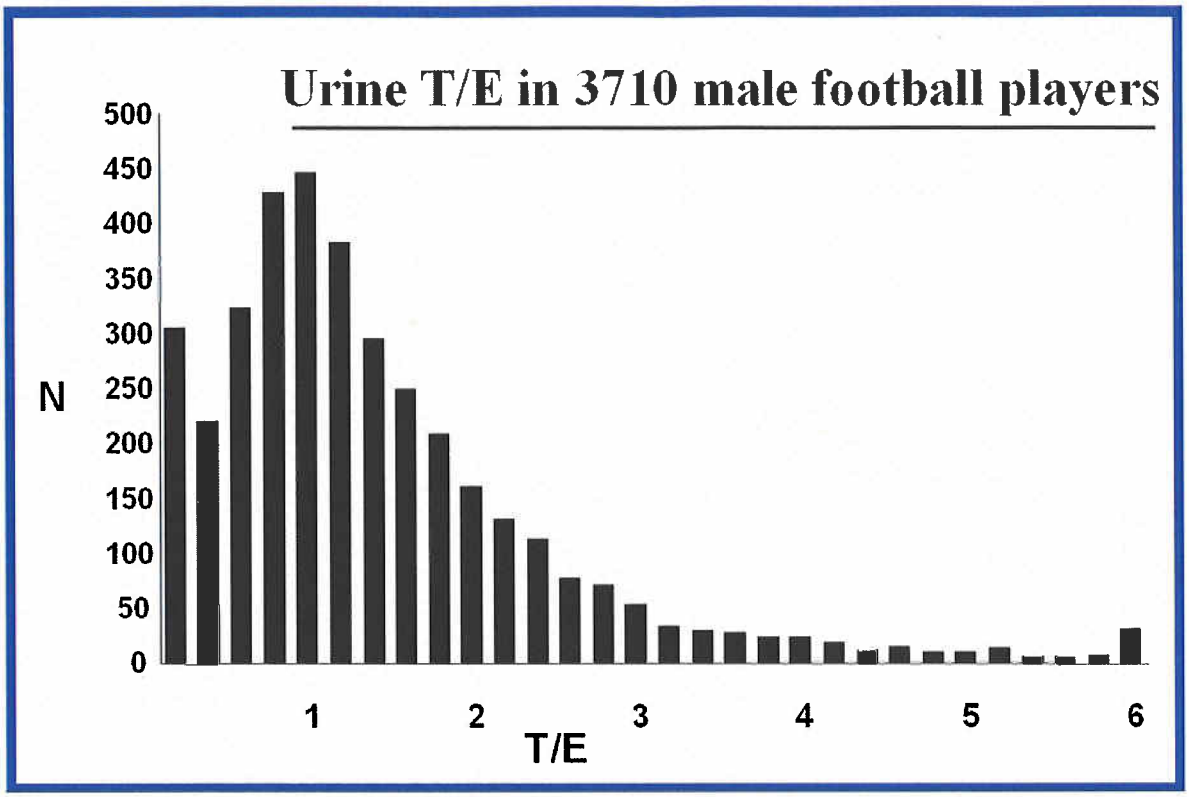
V. RESPONDENT'S T/E RATIO OF 11:1 SUPPORTS THE IRMS FINDING OF EXOGENOUS TESTOSTERONE.

A. Respondent's T/E ratio in Sample #995474 and T/E longitudinal profile are not consistent with normal human physiology.

122. In most normal males, the amount of testosterone and epitestosterone in urine is about the same; therefore, their urinary ratio of testosterone to epitestosterone (T/E ratio) is roughly 1:1. When pharmaceutical testosterone is taken and eliminated in the urine, the numerator (T) increases, and the T/E ratio increases. Since the 1984 Olympics, the T/E ratio has been used to screen for testosterone use. Adverse analytical findings are defined by a T/E cutoff of 4.

123. The T/E ratio in Respondent's A and B confirmation samples was 11.4:1 and 11.0:1 respectively. This is substantially higher than the WADA adverse analytical finding reporting criteria of 4:1 and, as Figure 19 illustrates, T/E ratios greater than 6:1 are very unusual in the normal population.

Figure 19



T/E <5.6 in 99% of subjects. *Issues in Detecting Abuse of Xenobiotic Anabolic Steroids and Testosterone by Analysis of Athletes' Urine* (Clin Chem, 43: 1280-1288, 1997) (Exhibit 40 at USADA 1171).

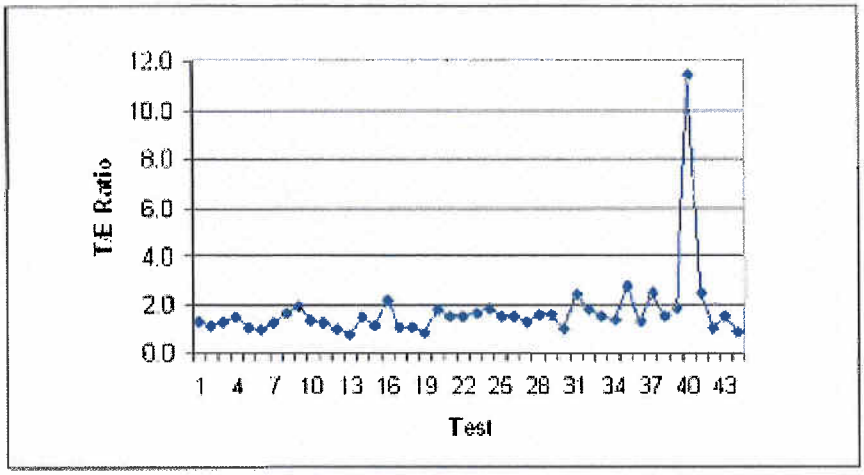
Most importantly, Respondent's T/E ratio of 11:1 on July 20, 2006 is entirely inconsistent with Respondent's historical T/E profile.

124. WADA Technical Document TD2004EAAS provides that even in the absence of a positive IRMS analysis, doping can be established when the T/E ratio in an athlete's single sample varies significantly from the athlete's historical T/E ratio. TD2004EAAS states that: "In males, the individual T/E values have been shown to vary from their mean value by less than 30%" (Exhibit 9, paragraph 5).

125. As instructed by TD2004EAAS, USADA has assembled an extensive longitudinal profile of Respondent's T/E ratios in 43 tests over the last four years. Tables setting forth these results are found at Exhibits 29 and 30. The mean of these 43 historical T/E ratios

(which excludes Sample #995474) is T/E 1.5:1. The T/E ratio of 11 in Respondent's Sample #995474 exceeds that mean by not 30% but rather by more than 600%. A time plot of Respondent's historical T/E values is set forth in Figure 20 below.

Figure 20



126. WADA Technical Document TD2004EAAS instructs that longitudinal studies should be evaluated as follows: "The individual basal T/E value should be determined from at least three test results, excluding the suspicious result under consideration. The mean, standard deviation and coefficient of variation (expressed in percent) should be calculated for those three basal values. If the suspicious test result, when compared to the basal value using appropriate statistical evaluation is found to be significantly different, that will constitute a proof of the administration of a source of testosterone" (Exhibit 9, paragraph 5).

127. The individual T/E basal values for Respondent are set forth on Exhibit 29. The mean, standard deviation and coefficient of variation of those values are:

Mean:	1.50
Standard Deviation:	0.46
Coefficient of Variation:	30.7% (Note, that this approximates the 30% normal range described in TD2004EAAS.)

The July 20, 2006 T/E ratio of 11 is more than 20 standard deviations from the mean.[8] There is no question that Respondent's T/E ratio of 11 on July 20, 2006 is clearly significantly different than the rest of his longitudinal profile.

B. <u>Description of the LNDD T/E ratio method.</u>

128. The method used by LNDD to measure T/E ratio was specifically included in its ISO certification (Exhibit 26, LNDD 0097).

EC24C	Urine	Analyse quantitative de la testostérone et de l'épitestostérone (molécules à seuil) (2) CD : Tir, Surface des ions majoritaires	Extraction SPE, dérivation TMS et analyse CG/SM IE SIM	Agilent CG6890 / MSD5973 Extraction : Cartouche C18/TEMOI Colonne : HP1 (25m-0,2mm-0,11µm)	EC24C-V.A.1 I-CONF-24C : -M-Ex-04b -M-An-27	Variation maximale admissible du rapport T/E = [20-50%]

129. LNDD screens urine samples for T/E as a part of its anabolic steroid screen by GC-MS. First, sample preparation includes steps such as the addition of an internal standard (methyltestosterone, for later reference), extraction, cleavage (hydrolysis) of sugars attached to the desired compounds by the body's biochemistry, and a chemical reaction with a reagent to attach a chemical to the desired compounds to make them easier to vaporize (derivatization as TMS). In the GC-MS screen, T and E are monitored by their molecular weight, ion 432. The expected retention times of T and E are approximately 15.2 and 14.3 minutes, respectively. The peaks corresponding to compounds are found by a computer integration program. The T/E ratio estimate is based on the peak area ratio. If the screen T/E is greater than the WADA cutoff of 4, then a T/E confirmation and an IRMS confirmation are both initiated.

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[8] Even if the lowest of Respondent's two T/E screen values (4.9:1) is used for comparison to the mean (to account for the fact that LNDD's T/E screening and confirmation methods are different), the July 20 T/E result would be more than 7 standard deviations from the mean. The statistical probability associated with 7 standard deviations is only a few occurrences in a trillion.

130. The purpose of the A sample T/E confirmation is to verify the T/E estimated in confirmation exceeds the WADA cutoff.

131. For T/E confirmation, two new urine aliquots are prepared, one with hydrolysis, one without. The aliquot without hydrolysis is used to measure "free" testosterone and epitestosterone as a check for sample deterioration.

132. To estimate the sample T (or E) concentrations, standard curves are prepared. In practice, the LNDD standard curves are made by analyzing three tubes containing urine spiked at known concentrations of T and E, side-by-side with the sample aliquots.

Concentrations (ng/mL)	T	E
Tube 1	30	5
Tube 2	180	30
Tube 3	360	60

The urine is prepared by collecting urine from a donor, extracting it with organic solvent to remove any potential free T or E, then spiking it with known amounts of reference standard T and E.

133. A different GC-MS time and temperature program is used for T/E confirmation (compared to the steroid screen GC program) to achieve better peak separation and therefore obtain a better estimate of peak area. The expected retention times of T and E are approximately 19.3 and 18.5 minutes, respectively.

134. From the GC-MS data, the peak areas of T and E relative to the internal standard methyltestosterone are estimated. The known relative peak areas correspond to known Y values. From these three experimental data points with known X and Y values, the curve is calculated by linear regression, a mathematical procedure that determines the line that fits the data best.

135. For the sample, the relative area of T (or E) to internal standard is determined experimentally. The estimated concentration is then calculated from the standard curve.

136. LNDD corrects T and E concentrations in order to express them as if the urine had a specific gravity of 1.020, using the equation from the WADA TD2004EAAS.

137. Thus three results are obtained from T/E confirmation: the estimated T/E (area ratio), and the estimated, corrected T and E concentrations.

138. For quality control purposes, a Blank Urine undergoes the assay side-by-side with the sample.

C. Respondent's defenses directed at LNDD's conclusion that the T/E ratio in Respondent's A and B samples were 11.4 and 11.0 respectively.

139. Before receiving Respondent's Trial Brief, USADA can only guess which defenses Respondent might choose to rely upon. However, based on Respondent's press campaign and Discovery Brief, several of the claims which it appears that Respondent will raise are addressed separately below.

D. Respondent's allegation: "The evidence of contamination-degradation of the sample."

140. Following sample collection, Respondent's A and B specimens were placed in a refrigerator and then in a cooler containing dry ice. That sealed cooler was transported by courier, helicopter and private plane to LNDD where it arrived within four hours of the completion of Respondent's sample collection (Exhibit 27 and Exhibit 24, USADA 0024).Upon receipt at LNDD, Respondent's A sample was put in Cold Room 1 (4 degrees Celsius); Respondent's B sample was put in Freezer 3 (-20 degrees Celsius), then moved on July 28, 2006 to Freezer 5 (-20 degrees Celsius) where it remained until the time of

the B sample opening. It is extraordinarily unlikely that sample degradation would occur in a sample under these conditions.

141. Respondent's degradation claim is based on Respondent's calculation that the ratio of free epitestosterone to total epitestosterone in Respondent's B sample was 7.7% which Respondent claims violates the requirements of WADA Technical Document TD2004EAAS. That document provides that to report an adverse analytical finding, the concentration of free testosterone and/or epitestosterone in the specimen is not to exceed 5% of the respective glucuroconjugates. The problem with Respondent's argument is that the amount of free epitestosterone which is the numerator in Respondent's ratio calculation (0.44 ng/ml), is far too small to be measured accurately by the GC/MS instrument. For example, the WADA minimum required performance level for the detection of epitestosterone is 2 ng/ml (Exhibit 10). No scientist with experience in GC/MS analysis would rely on a 0.44 ng/ml report of free epitestosterone value. In Respondent's A sample no free epitestosterone could be detected.

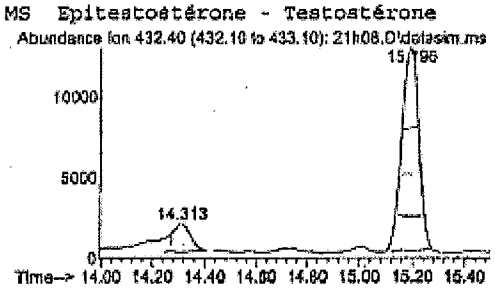
142. If there is too much free epitestosterone or testosterone in a sample, it may mean that other steroids have degraded into epitestosterone or testosterone and thus the amounts of epitestosterone and testosterone found in the sample are artificially high. That is important because epitestosterone is also expressly prohibited as a masking agent and a concentration of epitestosterone greater than 200 ng/ml is considered suspicious and triggers IRMS analysis (TD2004EAAS page 2, Exhibit 9). The reporting of an artificially high amount of epitestosterone has the opposite effect on the T/E ratio. The higher the amount of epitestosterone reported, the lower that makes the T/E ratio. Thus, if there was deterioration in the sample causing the production of excess epitestosterone, the only effect would have been to make Respondent's T/E ratio lower.

E. Respondent's allegation: "LNDD is incapable of calculating T/E ratios or total epitestosterone or testosterone values with the necessary certainty.

143. Respondent reaches this erroneous conclusion by mixing and matching data from the following sources: the A sample T/E screen (Exhibit 24, USADA page 0054), the repeat A sample T/E screen (Exhibit 24, USADA page 0057), the failed A sample T/E confirmation (Exhibit 24, USADA page 0223), and the successful A sample and B sample T/E confirmations (Exhibit 24, USADA page 0101 and Exhibit 25, USADA page 0288). It is not appropriate to mix and match the data in this way.

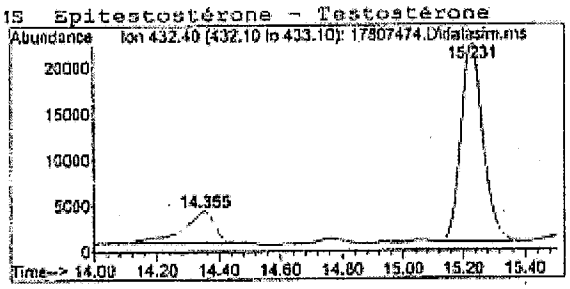
144. LNDD uses a different method for T/E screening than it does for T/E confirmation. Because it is only a screen, the T/E screening method is less accurate. This is consistent with Article 5.2.4.3 of the ISL which provides: "Since the objective of the confirmation assay is to accumulate additional information regarding an adverse finding, a Confirmation Procedure should have greater selectivity/discrimination than a Screening Procedure." The two times that the T/E screening method was employed by LNDD (the A screen and repeat A screen), the T/E ratios reported were consistent – A screen 4.9 (USADA 0054) and repeat A screen 5.1 (USADA 0057). However, in each case it is apparent that the screening method did not separate out a coeluting peak on the left shoulder of the epitestosterone peak that caused the amount of epitestosterone reported to be overstated.

4.9 T/E



USADA 0055

5.1 T/E



USADA 0058

This coeluting peak for epitestosterone was substantially eliminated during the more rigorous A and B sample confirmation method which produced more accurate results.

145. As reflected in Figure 21 below, the T, E and T/E ratios reported in the A and B confirmations are entirely consistent.

Figure 21. Consistency of "A" and "B" Confirmation T/E Ratios, Testosterone and Epitestosterone Concentrations

Date	USADA #	Sample #	T/E Ratio	T Concentration	EpiT Concentration
July 24, '06	0093	178/07 995474	11.4	61.4	5.2
Aug 6, '06	0277-78	178/07 995474	10.9	63.2	5.9
	0279-80	178/07 995474	11.0	61.6	5.8
	0281-82	178/07 995474	11.1	60.2	5.6

F. Respondent's allegation: "LNDD's laboratory documentation is riddled with errors."

146. Respondent points to numerous places in the documentation package where changes were made without the use of forensic correction technique. While this may not be consistent with best practice, it does not in any way rise to the level of a violation of the ISL. Respondent points to the forensic correction provisions found at Article 4.13.2.3 (Technical Records) of the ISO 17025 document. It should be noted that the Technical Records provision of ISO 17025 is not expressly incorporated into the ISL. The ISL in Article 5.3, Quality Management Process, specifically references those sections of ISO 17025 which are being incorporated into the ISL. A review of ISL Articles 5.3.7 through 5.3.14 reveals many Articles where the ISL specifically incorporates ISO 17025, e.g., the reference in ISL Article 5.8 to ISO Section 4.8. (See ISL Exhibit 8, Articles 5.3.7 through 5.3.14.)[9]

147. For each of the corrections identified by Respondent, the responsible laboratory technician can be identified. None of these corrections casts doubt on the analytical

[9] Note that the Section numbering between the version of ISO 17025 which was in effect at the time the ISL was adopted (Exhibit 8) and the 2005 version of ISO 17025 produced by Respondent (Exhibit 23) does not match up.

results. Even if failure to follow forensic correction techniques were a violation of the ISL, there is no difficulty in demonstrating that the corrections themselves were appropriate and did not cause Respondent's positive test.

148. In his Discovery Brief Respondent claims that "the documentation package contains numerous examples where the sample number is something other than "995474" (page 22). However, in Exhibit 49 to Respondent's Discovery Brief, which purports to detail all of the alleged documentation errors, only three cases of wrong sample numbers are identified.

149. Respondent's correct sample number is 995474. At page USADA 0024 (Exhibit 24) Respondent claims the sample number written is "995676." That is not correct. The technician wrote the correct number 995474; it is simply the case that the number "4" as she writes it can be mistaken for the number "6." This is apparent every time this technician wrote the number "4" throughout the documentation package.

150. Respondent identifies USADA 0008 as containing the wrong sample number 995475. It is true that the handwritten entry "995475" is incorrect. It is also ironic, as illustrated below, that in pointing this out, whoever prepared Exhibit 49 for Respondent also wrote the incorrect sample number for Respondent: "955474."

USADA 0008	ISO 4.12.2.3	1	Sample ID	In the middle of the page, second column, a sample is listed as 995475. Floyd's 17th digit number was 995474. This page is missing in the AFLD filing. This may be an effort to cover-up this error and malfeasance.

USADA 0008 is simply a handwritten summary form. Importantly, as reflected throughout the documentation package, Respondent's correct sample number was correctly identified each and every time his sample was placed on an instrument for analysis. The transposition error on USADA 0008 casts no doubt that LNDD's analysis was performed on Respondent's sample.

151. Sample numbers 995676 and 995475 were assigned to samples from other riders in the Tour de France. The other riders samples were received on days different from Respondent's sample (Exhibit 26, LNDD 0138 and LNDD 0144). To satisfy Respondent that there had not been a mix-up with another rider's sample, at Respondent's request, LNDD provided the LNDD report forms for the real Samples #995676 and #995475 to confirm that both samples were reported negative (Exhibit 26, LNDD 0379 and LNDD 0380).

152. The other instance where Respondent identifies an incorrect sample number in the documentation package is discussed in the following section.

G. Respondent's allegation: "Evidence of tampering with laboratory documents."

153. This claim by Respondent is based on the following handwritten changes to USADA page 0288 of the laboratory's B documentation package.

LNDD	ENREGISTREMENT	Code : E-FCR-04B2 Version : A Date : 03/08/2006 Page : 1/1

FICHE D'ANALYSE / RESULTAT - CONFIRMATION SEMI-QUANTITATIVE T/E (trois aliquotes)

Paraphe :

Echantillon : 478/07 99/474 Dilution : 1/ 1

Ion de quantification Testo et Epitesto : 432 Ion de quantification SI : 301

Concentration de la référence 1 : Testosterone: 30 Epitestosterone : 5 T/E théorique : 6

Concentration de la référence 2 : Testostérone: 180 Epitestosterone : 30 T/E théorique : 6

Concentration de la référence 3 : Testostérone: 360 Epitestosterone : 60 T/E théorique : 6

Fichier		Surface du SI	Surface Testosterone	Surface Epitestosterone
REF1	REF1TE	3782021	1845917	294592
REF2	REF2TE	3011193	7860237	1324358
REF3	REF3TE	3783290	20557109	3442296
1780774A		3971127	3733052	342595
1780774B		3356149	3079122	279871
1780774C		4098783	3670090	329392

RESULTAT DE L'ECHANTILLON

Fichier	Concentration Testosterone		Concentration Epitestostérone		Rapport T/E en surface
1780774A	63,2	ng/mL	5,9	ng/mL	10,9
1780774B	61,6	ng/mL	5,8	ng/mL	11,0
1780774C	60,2	ng/mL	5,6	ng/mL	11,1
Moyenne	61,7	ng/mL	5,7	ng/mL	11,0
Ecart type	1,5	ng/mL	0,2	ng/mL	0,1
Valeur finale	61,7	ng/mL	5,7	ng/mL	

Partie à remplir par le responsable

Seuil de déclaration du rapport T/E (en surface) : 4

Incertitude (liée à la méthode) pour le rapport T/E : 30% pour l'Epitestosterone : 30% pour la Testosterone : 20%

Valeur basse du rapport T/E : 7.7 Résultat : Anormal : X

Valeur haute du rapport T/E : 14.3 Inclassable :

Négatif :

Correction des concentrations en Testosterone et Epitestosterone par la densité (cf doc E-INC-03) :

Densité affichée	1.025
Numéro du réfractomètre	9
Densité corrigée :	1.025
Facteur de correction	0.74
Concentration corrigée de Testosterone	45.7 ng/mL
Concentration corrigée d'Epitestosterone	4.2 ng/mL

PARAPHE

Ecart n° :

Cet enregistrement est à archiver dans le dossier de confirmation

60

154. It is true that Respondent's sample number is typed incorrectly at the top of the form.

155. A search of LNDD's records back to 2001 does not reflect the receipt of any sample numbered 994474.

156. USADA 0288 is a manually prepared summary table of the results generated by the GC/MS instrument from the T/E analysis of Sample #995474. The analytical results reflected on this table come from the instrument reports found at pages USADA 0277 through USADA 0282 of the documentation package (Exhibit 25). Each one of these instrument reports correctly identifies Respondent's sample number. In transposing the information from the instrument reports to the top of the summary form found at USADA page 0288, there was a mistake in transposing the number of Respondent's sample. It is important to note, however, the laboratory sample number "1780774" is written correctly on USADA 0288 all six times sample data is presented. To further illustrate that the T/E B sample confirmation report found on USADA 0288 is from Respondent's B sample, Exhibit 32b tracks sample number 995474 from the time ten witnesses agreed the bottle seal was intact through sample preparation and GC/MS analysis to the summary of results on page USADA 0288.

157. The original laboratory documentation package in LNDD's files does not include the notation correcting the sample number. There is no copy of USADA page 0288 in LNDD's files where this correction has been made. The documentation package provided by LNDD through USADA to Respondent on August 30, 2006 is identical to the original document in LNDD's files and shows no correction. The laboratory documentation package was provided by LNDD to the supervising agency, the AFLD, after the documentation package was provided to Respondent. The documentation package which LNDD provided to AFLD was identical to

the package provided to Respondent and contained no correction to the sample number on page 0288. It is apparent that sometime after the sample number error was brought to everyone's attention by Respondent in Dr. Arnie Baker's PowerPoint presentation (Exhibit 33) that someone at AFLD simply corrected the obvious mistake. There was no intent or opportunity to deceive. Since Respondent had already been provided an accurate copy of the original documents by LNDD through USADA and since he had already recognized the mistake on page USADA 0288, there would have been no sense in anyone trying to alter the document to deceive someone. There was no one to be fooled.

VI. ADDITIONAL EVIDENCE NOT YET AVAILABLE.

158. As the Panel is well aware, IRMS analysis on Respondent's other seven Tour de France samples is scheduled to commence today, April 16, 2007. The results of that analysis, positive or negative, are likely to be highly relevant to this case.

159. USADA has served discovery on Respondent with responses due by April 16, 2007. Part of that discovery seeks to address various defenses which Respondent has raised in the press. However, USADA has also asked Respondent to provide the results of routine blood tests which UCI performs on riders. USADA has been advised by UCI that it provided all of his UCI blood testing data to Respondent early in this case. USADA is only able to get this information from Respondent. This information could be of interest because one side effect of testosterone administration can be increases in hemoglobin.

160. USADA will supplement its brief on these two issues at such time as the additional information is obtained.

VII. SANCTIONS AND CONSEQUENCES.

161. Under Chapter 10 of the UCI rules, the consequences of Respondent's anti-doping rule violation are disqualification of Respondent's results in the Tour de France and in any competitions in which Respondent participated subsequent to the Tour de France and two years ineligibility from the date of the hearing.

VIII. CONCLUSION

For all of the foregoing reasons, USADA respectfully submits that the evidence in this case leads the Panel to the same conclusion reached by the arbitrators in Susin v. FINA:

> "151. For the following reasons, the Panel has concluded that FINA has satisfied its burden of proving that the Appellant committed a doping offence under FINA Rule DC 2.1(a):
>
> "(a) IRMS analysis provides direct and conclusive evidence of an exogenous administration of the prohibited substance testosterone by the Appellant;
>
> "(b) the Panel is entitled to rely upon the IRMS analysis in the circumstances of this case; and
>
> "(c) the Appellant's elevated T/E ratio and longitudinal hormonal study provide corroborative evidence of an exogenous administration of testosterone."

Respectfully submitted this 16th day of April, 2007.

United States Anti-Doping Agency

Richard R. Young
Matthew S. Barnett
Holme Roberts & Owen LLP
90 South Cascade Avenue, Suite 1300
Colorado Springs, CO 80903

Travis T. Tygart
General Counsel
1330 Quail Lake Loop, Suite 260
Colorado Springs, CO 80906

Attorneys for the United States Anti-Doping Agency

CERTIFICATE OF SERVICE

The undersigned hereby certifies that on this 16th day of April, 2007, a true and correct copy of the foregoing **PRE-HEARING BRIEF OF UNITED STATES ANTI-DOPING AGENCY** was served by Electronic Mail and Federal Express, as follows:

Richard H. McLaren, Esq.
Innovative Dispute Resolution, Ltd.
c/o McKenzie Lake Lawyers, LLP
300 Dundas Street
London, Ontario N6B 1T6
CANADA
E-mail: mclaren@mckenzielake.com

Christopher L. Campbell, Esq.
Chapman & Intrieri
2236 Mariner Square Drive,Ste. 300
Alameda, CA 94501
E-mail: ccampbell@chapmanandintrieri.com

Patrice M. Brunet, Esq.
1010 DeLa Gauchetiere West, #2260
Montreal, Quebec H3B2N2
CANADA
E-mail: Pbrunet@brunetavocats.com

Maurice M. Suh
Gibson, Dunn & Crutcher LLP
333 South Grand Avenue
Los Angeles, CA 90071-3197
Email: msuh@gibsondunn.com

Howard L. Jacobs, Esq.
5210 Lewis Road
Suite 5
Agoura Hills, CA 91301
Email: howard.jacobs@yahoo.com

Anita L Smith